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# Evoked potentials in the diagnostics of central nervous system disorders in diabetic patients

## Abstract

**Background.** Patients with diabetes suffer central nervous system (CNS) damage which is difficult to diagnose. Examination of evoked potentials (EP) — bioelectric responses of the nervous system to external sensory (SEP), acoustic (BAEP) or visual (VEP) stimuli — may be used to assess CNS dysfunction.

**Material and methods.** We performed VEP and SEP studies in the median (SEPm) and the tibial (SEPt) nerves in 90 patients with type 1 and 2 diabetes using the four-channel device Premiere[plus]. EP were estimated according to the presence of peripheral polyneuropathy, glycemic control, sex and diabetes type. The diagnosis of peripheral polyneuropathy was established by clinical examination according to the Neuropathy Disability Scale (NDS).

**Results.** Abnormal SEP were found in 25% of patients without the clinical symptoms of neuropathy. Abnormal SEPt were found in 64.4% of patients and abnormal SEPm and VEP in 31.1% of patients. Abnormal VEP were more common in patients with clinical signs of peripheral polyneuropathy ($P = 0.004$), insufficient glycaemic control ($P < 0.02$), type 2 diabetes ($P = 0.004$, right eye; $P = 0.001$, left eye) and in the elderly patients ($P < 0.001$). Abnormal SEPt ($P < 0.05$) and SEPm ($P < 0.01$) correlated with age and SEPt additionally correlated with the presence of peripheral polyneuropathy (P 0.0053).

**Conclusions.** Examination of evoked potential in patients with diabetes allows to diagnose subclinical CNS damage. The more frequent occurrence of abnormal tibial verus median nerve bioelectric response probably results from the difference in length between the two nerves. Examination of VEP seems to be more useful for the evaluation of the effects glycaemic control on CNS function than examination of evoked potentials from the peripheral nerves.

**key words: evoked potentials, diabetes mellitus, central nervous system**

## Introduction

Diabetes may cause damage in both the peripheral and the central nervous systems (CNS). Although according to researchers, pathological factors promoting the development of central and peripheral neuropathy seem similar, few studies of this topic have been published so far [1–8]. It is believed that both types of disorder are triggered by microcirculation changes and metabolic factors [1, 2, 9–15]. Autoimmune and inflammatory mechanisms are also taken into account [16–19]. Early CSN damage is difficult to diagnose, and its detection is only possible through electrophysiologic and psychomotor testing. Central nervous systems dysfunction may be evaluated by the examination of evoked potentials — bioelectric responses of the nervous system to sensory (SEP), acoustic (BAER) and visual (VEP) stimuli. Motor evoked potentials are also distinguished, which are a response to extracranial magnetic stimulation of the motor cortex or transdermal stimulation of nerve roots and trunks [20, 21]. The aim of our study was to establish the usefulness of evoked potential testing in the diagnostics of central nervous system disorders in patients with diabetes in light of the selected clinical parameters.

## Material and methods

Ninety patients with type 1 or type 2 diabetes mellitus hospitalised at the Chair and Clinic of Endocrinology and

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Diabetology, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland, were included in the study. Patients with a history of CNS diseases, manifestations of diabetic mononeuropathy, proximal neuropathy or carpal tunnel syndrome were excluded from the study.

Table 1 summarises patient characteristics.

The patients underwent examinations of visual (VEP) and somatosensory evoked potentials (SEP) from the median (SEPm) and the tibial (SEPt) nerves. EP studies were performed using the four-channel Premiere$^{plus}$ from Medelec (TECA) in standard environment, in a room with a temperature of approximately 25°C. VEP were recorded using subcutaneous needle electrodes placed at $O_z$ with the reference electrode at Fz (according to the 10–20 system). The left followed by the right eye were stimulated twice using a fully reversible checker board pattern of 100% contrast. The stimulation was presented on a monitor. The frequency of the pattern change was 2 Hz and the viewing angle of individual elements of the pattern was 70'. We evaluated the latency of the main wave P100, its amplitude (N75-P100 or P100-N145), morphology and the interocular difference in latency and amplitudes. In order to evaluate SEPm, we stimulated the right median nerve in the wrist. The recording was performed using subcutaneous needle electrodes placed on the cranium over the cortical representation of the hand contralaterally to C4' stimulation and superficial cup electrodes at Erb point ipsilaterally to the stimulation and over the osseous process of the 6th cervical vertebra. We evaluated the latency of the following N components: distal response N9, spinal response N13 and cortical response N19, as well as their amplitudes (peak-peak) and N13-N19 interlatency. Examination of SEPt was performed by stimulating the tibial nerve at the medial ankle. The recording was performed using subcutaneous needle electrodes placed on the cranium at Cz' and superficial cup electrodes placed over the osseous process of the 12th thoracic vertebra and in the popliteal fossa ipsilaterally to the stimulation. The reference electrodes were placed at Fz, over the iliac spine contralaterally and in the popliteal fossa. We evaluated the latency of the following components: peripheral response N8, spinal response N22 and cortical response P40, as well as their amplitudes (peak-peak) and N22-P40 interlatency.

The results were considered abnormal where no response was evoked or where the response evoked had abnormal parameters compared to the normal values adopted by the laboratory.

The evoked potentials were evaluated depending on the presence of peripheral polyneuropathy, sex, diabetes type and glycaemic control. The diagnosis and severity of peripheral neuropathy were established on the basis of a clinical examination according to a modified Neuropathy Disability Scale (NDS) [22–25]. The analysis depending on the degree of glycaemic control was performed in two groups, with "relatively good" glycaemic control and with "insufficient" glycaemic control. Due to the low percentage (11.1%) of patients with good glycaemic control [defined as glycated haemoglobin ($HbA_{1c}$) levels of ≤ 6.5% according to the Polish Diabetes Association], the level of ≤ 7.5% was adopted as an exponent of relatively good metabolic control of diabetes in the present work.

The study had been approved by the Bioethics Committee of Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland.

**Table 1.** Characteristics of the study group

| Parameter | Unit of measurement | Mean ± SD | |
|---|---|---|---|
| Age | Years | 46.4 ± 12.4 | |
| Duration of diabetes | Years | 12.7 ± 9.5 | |
| $HbA_{1c}$ | % | 9.04 ± 2.1 | |
| | n | (%) | |
| Female sex | 40 | 44.4 | |
| Type 1 diabetes | 57 | 63.3 | |
| Hypertension | 38 | 42.2 | |
| Diabetic retinopathy | 42 | 46.6 | |
| Diabetic nephropathy | 25 | 27.8 | |
| Peripheral polyneuropathy | 54 | 60 | |
| — mild | 26 | 28.9 | 100 |
| — moderate | 22 | 24.4 | |
| — severe | 6 | 6.7 | |

## Statistical analysis

The parameters with gaussian distribution (according to the Kolmogorov-Smirnov test) were analysed with the *t*-Student test while the parameters with non-gaussian distribution were analysed using the non-parametric U Mann-Whitney test and the chi-square goodness-of-fit test. Analysis of variance (ANOVA) was performed. Pearson or Spearman correlation coefficients were determined. The results were presented as means and standard deviations. Differences at the P value of less than 0.05 were considered statistically significant.

## Results

The results are summarised in Table 2. Abnormal SEPt were most common (58.0–64.4% of patients), while abnormal SEPm and VEP were observed in 28 patients (31.1%).

**Table 2.** Evoked potentials according to the presence of peripheral polyneuropathy, sex, diabetes type and glycaemic control (significantly different values are placed in the grey boxes). L — latency (ms); A — amplitude ($\mu$V); % — percentage of abnormalities (%); VEP — visual evoked potentials; OD — right eye; OS — left eye; SEPm — median nerve stimulation somatosensory evoked potentials; N9 — distal (Erb) peak; N13 — spinal peak; N19 — cortical peak; SEPt — tibial nerve stimulation somatosensory potentials ($SEP_t$); N8 — distal peak; N22 — spinal peak; P40 — cortical peak; OCP — central conduction time (CCT)

| | | Polyneuropathy | | | No polyneuropathy | | | Men | | | Women | | | Type 1 | | | Type 2 | | | Controlled glycaemia | | | Uncontrolled glycaemia | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | % | L | A | % | L | A | % | L | A | % | L | A | % | L | A | % | L | A | % | L | A | % | L | A |
| VEP | OD | 42.6 | 109.6 ±8.48 | 7.14 ±2.25 | 13.9 | 105.7 ±7.02 | 9.13 ± 2.76 | 28 | 107.0 ± 7.04 | 8.04 ± 2.91 | 35 | 109.3 ±9.20 | 7.80 ±2.28 | 31.6 | 108.3 ±7.60 | 8.53 ±2.68 | 30.3 | 107.6 ±9.03 | 6.90 ±2.25 | 10.7 | 105.7 ±6.53 | 8.09 ±2.49 | 40.3 | 109.1 ±8.57 | 7.86 ±2.72 |
| | OS | | 109.3 ±8.70 | 6.88 ±2.57 | | 105.3 ±6.42 | 9.86 ±3.23 | | 107.2 ±7.00 | 8.26 ±3.44 | | 108.4 ±9.27 | 7.83 ±2.88 | | 108.2 ±8.38 | 8.89 ±3.34 | | 106.8 ±6.65 | 6.65 ±2.35 | | 105.4 ±5.46 | 8.51 ±3.37 | | 108.8 ±8.84 | 7.87 ±3.12 |
| SEPt | N9 | | 9.25 ±1.36 | 2.24 ±0.99 | | 8.93 ±0.99 | 2.74 ±1.18 | | 9.34 ±1.12 | 2.43 ±0.82 | | 8.86 ±1.08 | 2.52 ±1.14 | | 9.24 ±1.19 | 2.54 ±1.05 | | 8.67 ±0.74 | 2.28 ±0.67 | | 8.95 ±0.99 | 2.42 ±0.89 | | 9.16 ±1.17 | 2.50 ±1.01 |
| | N13 | 35 | 13.33 ±0.91 | 2.56 ±0.65 | 25 | 13.28 ±0.67 | 2.76 ±0.45 | 36 | 13.59 ±0.76 | 2.56 ±0.59 | 25 | 12.89 ±0.71 | 2.69 ±0.52 | 31.6 | 13.39 ±0.88 | 2.66 ±0.61 | 30.3 | 13.03 ±0.50 | 2.51 ±0.40 | 28.5 | 13.22 ±0.84 | 2.56 ±0.44 | 32.2 | 13.32 ±0.80 | 2.65 ±0.62 |
| | N19 | | 19.84 ±1.90 | 2.99 ±0.84 | | 19.69 ±1.40 | 3.30 ±0.73 | | 19.95 ±1.57 | 3.09 ±0.85 | | 19.04 ±1.21 | 3.09 ±0.76 | | 19.66 ±1.53 | 3.19 ±0.88 | | 19.28 ±1.35 | 2.83 ±0.49 | | 19.60 ±1.60 | 2.99 ±0.54 | | 19.54 ±1.43 | 3.14 ±0.92 |
| | OCP | | 6.51 ±1.51 | | | 6.41 ±1.35 | | | 6.36 ±1.35 | | | 6.15 ±0.81 | | | 6.28 ±1.03 | | | 6.26 ±1.44 | | | 6.37 ±1.46 | | | 6.21 ±0.94 | |
| SEPm | N8 | | 10.97 ±1.31 | 1.52 ±0.66 | | 9.86 ±1.49 | 2.35 ±1.28 | | 10.60 ±1.34 | 1.93 ±0.94 | | 10.31 ±1.67 | 1.83 ±1.23 | | 10.30 ±1.49 | 2.01 ±1.07 | | 10.94 ±1.41 | 1.56 ±0.99 | | 10.33 ±1.47 | 2.07 ±0.98 | | 10.55 ±1.51 | 1.78 ±1.11 |
| | N22 | 75.9 | 21.76 ±1.12 | 2.42 ±0.65 | 47.2 | 21.63 ±1.16 | 2.77 ±0.46 | 64 | 22.09 ±1.05 | 2.49 ±0,60 | 65 | 21.19 ±1.01 | 2.70 ±0.58 | 59.6 | 21.70 ±1.03 | 2.62 ±0.56 | 72.7 | 21.71 ±1.38 | 2.48 ±0.68 | 50 | 21.60 ±1.01 | 2.63 ±0.48 | 71 | 21.76 ±1.19 | 2.55 ±0.65 |
| | P40 | | 41.09 ±1.95 | 3.31 ±1.27 | | 40.78 ±2.00 | 3.57 ±0.83 | | 41.90 ±1.85 | 3.44 ±0.91 | | 39.70 ±1.32 | 3.41 ±1.30 | | 40.93 ±1.88 | 3.54 ±0.85 | | 41.01 ±2.22 | 3.13 ±1.54 | | 40.84 ±2.06 | 3.41 ±0.84 | | 41.01 ±1.93 | 3.43 ±1.21 |
| | OCP | | 19.30 ±1.75 | | | 19.15 ±1.55 | | | 19.78 ±1.84 | | | 18.52 ±1.03 | | | 19.21 ±1.67 | | | 19.30 ±1.67 | | | 19.25 ±1.76 | | | 19.22 ±1.61 | |

### Evaluation of the evoked potentials relative to the presence and severity of peripheral polyneuropathy

Abnormal SEPt and VEP were significantly more common in patients with clinical manifestations of polyneuropathy than in patients without these manifestations (47.2% *vs*. 75.9%, P = 0.0053 and 13.9% *vs*. 42.6%, P = 0.004, respectively). Abnormal SEPm were found in 35% and 25% patients with and without clinical manifestations of polyneuropathy, respectively. The mean latencies of N9, N13 and N19 and the central conduction time (CCT) were longer, and the amplitudes were lower in patients with clinical manifestations versus asymptomatic patients. The differences in the amplitude of N9 and N19 between the two subgroups were statistically significant (P = 0.0382 *vs.* P = 0.0315). The increased severity of neuropathy was paralleled by reduced amplitude of N9 (r = –0.3829; P = 0.01), N13 (r = –0.4287; P < 0.01) and N19 (r = –0.3151; P < 0.05), and the increased latency of N9 (r = 0.353; P < 0.02) and N19 (r = 0.3286; P = 0.021). Patients suffering from a severe form of neuropathy demonstrated longer mean latencies of response from N9, N13 and N19 than others. The longest mean CCT was found in patients with severe neuropathy. The mean amplitude of N13 was significantly higher than the mean amplitude in patients without polyneuropathy or patients with mild neuropathy versus patients with severe polyneuropathy (P = 0.0289 *vs.* P = 0.0161).

Abnormal SEPt were most commonly found in patients with moderate and severe polyneuropathy (respectively: 90.9% and 90.2%, P = 0.008). The mean amplitudes of N8 and N22 in patients with clinical manifestations of polyneuropathy were significantly lower than those in patients without clinical manifestations of polyneuropathy (P = 0.0071 *vs.* P = 0.0021), while the mean latency of N8 was significantly higher in patients with polyneuropathy (P = 0.00007). The mean latencies of the other waves were longer, and amplitudes lower in patients with clinical manifestations of polyneuropathy. With an increasing severity of polyneuropathy on clinical examination we found a significant reduction of amplitude in the peripheral response N8 (r = –0.3433; P = 0.02), spinal response N22 (r = –0.3874; P < 0.01) and cortical response P40 (r = –0.2983; P < 0.05), and an increased latency of the response form N8 (r = 0.4877; P < 0.001) and N22 (r = 0.3075; P < 0.05). The mean amplitude of N8 was the highest in the subgroup of patients without clinical manifestations of polyneuropathy, and the lowest in the subgroup with severe polyneuropathy. The differences between the mean amplitudes and latencies of N8 depending on the severity of polyneuropathy were statistically significant (H = 8.5860; P = 0.0001 *vs*. H = 20.5353; P = 0.0001).

In the VEP study, the mean latencies and amplitudes of the P100 response from the right eye (OD) and the left eye (OS) did not differ significantly in the study group. The mean latencies of P100 from OD and OS were significantly longer in patients with clinical manifestations of polyneuropathy than in patients without clinical manifestations (P = 0.00276 *vs.* P = 0.00218), while the mean amplitudes of P100 from OD and OS were significantly lower in patients with signs of polyneuropathy (P = 0.0003 *vs*. P < 0.0001).

With an increasing severity of polyneuropathy we found a significant reduction of the amplitude of P100 (OD: r = –0.4429; P = 0.001; OS: r = –0.4777; P = 0.001). The mean latency of P100 was the shortest in the subgroup of patients without clinical manifestations of polyneuropathy and the longest the subgroup of patients with severe polyneuropathy. The mean amplitude of the wave from OD in patients without clinical manifestations of polyneuropathy was significantly higher than the mean values in patients with mild (P = 0.0377) and severe (P = 0.0051) polyneuropathy. In the latter subgroup, the mean amplitude of P100 form OD was the lowest. The mean amplitude of P100 from OS in patients without clinical manifestations of polyneuropathy was significantly higher than the mean amplitudes in patients with mild (P = 0.0107), moderate (P = 0.0205) and severe (P = 0.0040) polyneuropathy, who also presented with the lowest amplitude.

### Evaluation of the evoked potentials relative to sex

No statistically significant differences were found in the incidence of abnormal SEPt, SEPm or VEP between women and men. The mean latencies of the distal, spinal and cortical responses and the central conduction time were longer in men than in women. The differences in the mean latencies of N13 (P = 0.008) and N19 (P = 0.019) were statistically significant. The mean latencies of N8, N22 and P40, and the CCT were also longer in men than in women. Statistically significant differences were found between the latencies of N22 (P = 0.002), P40 (P = 0.000002) and CCT (P = 0.003).

### Evaluation of the evoked potentials relative to the type of diabetes

Abnormal SEPt were the most common. They were demonstrated in 34 (59.6%) patients with type 1 diabetes and 24 (72.7%) patients with type 2 diabetes. Abnormal SEPm and VEP were recorded in 18 (31.6%) patients with type 1 diabetes and 10 (30.3%) patients with type 2 diabetes. The differences in the incidence of abnormal results were not statistically significant. The mean latencies and amplitudes of SEPm and SEPt did not differ significantly between

type 1 and type 2 diabetics. The mean amplitudes of VEP from the P100 response in both OD and OS were statistically lower in patients with type 2 diabetes ($P = 0.004$ and $P = 0.001$).

### Evaluation of the evoked potentials relative to glycaemic control

In patients with insufficient glycaemic control there was a significantly higher incidence of abnormal VEP ($P < 0.02$). The increased $HbA_{1c}$ was parallel by increased latency of P100 (OD: $r = 0.4985$; $P < 0.001$; OS: $r = 0.5551$; $P < 0.001$). The mean latencies of P100 were longer and the mean amplitudes were lower in patients with insufficient glycaemic control compared to patients with relatively good glycaemic control. The incidence of abnormal SEPm and SEPt did not differ significantly between patients with insufficient glycaemic control and patients with good glycaemic control.

### Evaluation of the evoked potentials relative to the patients' age and duration of illness

With increasing age, there was a significant reduction of the amplitude of N9 ($r = –0.4182$; $P < 0.01$), N19 ($r = –0.4248$; $P < 0.01$), peripheral response N8 ($r = –0.3786$; $P < 0.01$), spinal response N22 ($r = –0.3165$; $P < 0.05$) and cortical response P40 ($r = –0.316$; $P < 0.05$). There was also a significant increase of the latency of the peripheral response N8 ($r = 0.3233$; $P < 0.05$). No significant correlations between the other parameters and the age and duration of illness were found. VEP studies demonstrated that increased age was paralleled by reduced amplitudes of P100 (OD: $r = –0.5131$; $P < 0.001$; OS: $r = –5128$; $P < 0.001$). No significant correlations between the duration of illness and the latency or amplitude of P100 were found.

## Discussion

Abnormal SEP are reported in 28% to 84% of diabetic patients [4, 26–34]. Such considerable differences result from the selection of material and the adopted method. The percentage tends to increase when distal responses are also taken into account, especially in patients with clinical manifestations of symmetric peripheral polyneuropathy. Despite the fact that the research so far has suggested multifocal pattern of CNS dysfunction, it has failed to establish any correlation between peripheral and central nervous system damage in patients with diabetes. Some of the cited researchers evaluated spinal and cortical responses only. We, on the other hand, evaluated peripheral as well as spinal and cortical responses. The higher percentage of abnormal SEP from the tibial nerve (64%) compared to the median nerve (31%) is most probably related to the higher length of the nerve fibres in the lower extremities and, as a result, a higher susceptibility to injury. While this percentage was higher in patients with clinical manifestations of symmetrical peripheral polyneuropathy, it is worthy of noting that SEP in patients without polyneuropathy were also abnormal (47% and 25%). The abnormalities mainly concerned peripheral responses, although the reduction of amplitude and the increase of latency of the cortical wave along with the increased severity of polyneuropathy were also significant. Our findings are consistent with those by Ziegler, Comi, Fierro and Pozzessere [29, 33–36]. Kondo et al. reported positive correlations between the central conduction time from stimulation of the median nerve and the motor conduction velocity in the median nerve [26]. Celiker reported a similar percentage of abnormal SEP in patients without clinical manifestations of polyneuropathy, which may suggest that the peripheral and the central nervous systems are affected independently in patients with diabetes [10]. Similar conclusions were drawn by Sartucci, Palma and Suzuki [37–39].

In our study, we found a non-significantly higher incidence of abnormal SEP in patients with insufficient glycaemic control. Some researchers also emphasise the relationship between abnormal SEP and insufficient metabolic control, while others point to the increased number of SEP abnormalities with time despite the improved glycaemic control [26, 29, 32–34, 40, 41].

Similarly to other authors, we demonstrated reduced amplitudes of individual waves with age [14, 34]. It is believed that age-related SEP changes are caused by reduced numbers of myelinated fibres in nerve roots and the spinal cord and that they result from degenerative changes in the posterior columns [14, 42]. It is therefore difficult to establish unequivocally any relationship between these changes and diabetes.

We observed longer latencies of individual waves in the group of men, which was most probably related with the significantly higher mean height than in women (172 cm *vs.* 161 cm, $P < 0.01$) [29, 34, 36].

Palacz et al. reported abnormal VEP in 39% of patients with diabetes, 80% of whom had no changes in the fundus suggesting that these abnormalities could have been caused by pathologies coexisting in the optic nerve or further along the visual pathway. These researchers concluded that VEP were a valuable complement of electroretinography in the ophthalmologic evaluation of patients with diabetes because they allowed to diagnose central neuropathy and optic nerve changes [43].

A similar conclusion was arrived at by Parisi when he analysed VEP changes in patients in whom clinical retinopathy had not yet developed. He believes, however, that the VEP picture is determined independently by both retinal and extraretinal changes present in diabetic patients [44]. Many authors emphasise the presence of abnormal VEP in patients with new-onset insulin-dependent diabetes mellitus [33, 45–48]. The absence of changes in the electroretinogram or oscillation potentials in these patients suggests normal function of the external layers of the retina and the macula [47]. The abnormal function of the optic nerve in diabetic patients is probably caused by ischaemic or demyelinisation changes, as evidenced by the prolongation of P100 latency and confirmed by MRI. Another cause may be the pathology of the insulin neuritis type, similar to the one found in proliferative retinopathy [46, 49]. The authors unanimously emphasise that VEP are a valuable method in the diagnostics of subclinical central nervous system damage in patients with diabetes [4, 10, 11, 29, 36, 44, 46, 48, 50, 59].

We found abnormal visual evoked potentials (absence, prolonged latency of P100, reduced amplitude or prolonged interocular interlatency compared to the adopted standards) in 31% of the patients. Similar findings are reported by Cirillo, Algan, Comi and Fierro [10, 11, 36, 50, 52]. We found a significantly higher incidence of abnormal VEP in patients with clinical manifestations of polyneuropathy, although these changes were also present in 14% of patients without clinical manifestations of polyneuropathy. The abnormalities consisted in a prolonged latency of P100 and a reduced amplitude. A higher incidence of abnormal VEP in patients with clinical manifestations of polyneuropathy were also reported by Fierro, Yaltkaya and Mariani [29, 36, 54, 59]. Some authors point to the early appearance of VEP pathologies in young diabetic patients without other signs of nervous system damage and explain this fact by insufficient metabolic control and the high incidence of hypoglycaemic episodes, which impair the energy metabolism of the brain [10, 11, 29, 36, 46, 57, 60, 61]. In our patients, we found a higher incidence of abnormal VEPs in patients with insufficient glycaemic control. This is consistent with findings by other authors. Fierro et al. investigated 30 patients with type 1 diabetes and $HbA_{1c}$ > 8%. They diagnosed abnormal VEPs in 26% of patients. This percentage was reduced to 16% after one year of strict control and good glycaemic control confirmed by a reduction of $HbA_{1c}$ [29]. Resolution of VEP changes following a period of good metabolic control was also reported by Verotti [48]. Mariani also emphasises the relationship between VEP study results and glycaemic control [54]. These findings may suggest an effect of glycaemic control on VEPs and point to the reversibility of these changes. This suggests that these abnormalities may in part be functional in nature.

## Conclusions

1. Evoked potential testing enables a diagnosis and objective evaluation of central nervous system damage in the subclinical phase.
2. Evoked potential abnormalities are more pronounced in patients with clinical manifestations of symmetrical peripheral polyneuropathy. The abnormalities were the most common in the case of the tibial nerve, which was most probably related to the length of the nerve.
3. Visual evoked potentials seem to be the most useful tool in the evaluation of the effects of glycaemic control on CNS as compared to evoked potentials obtained as a result of stimulation of peripheral nerves.

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