Visual evoked potentials in idiopathic intracranial hypertension

Anat Kesler, Veronika Vakhapova, Amos D. Korczyn, Vivian E. Drory

1. Introduction

Idiopathic intracranial hypertension (IIH), or pseudotumor cerebri, is a disorder associated with increased intracranial pressure with no clinical, laboratory or radiological evidence of an intracranial space-occupying lesion [1–3]. Patients with IIH and papilledema may go on to develop visual loss, and therefore should be followed at regular intervals to detect early evidence of optic neuropathy. At present, the recommended examinations are purely clinical, consisting of visual acuity, optic disc appearance and visual field examination.

This study was undertaken in an attempt to examine the value of visual evoked potentials (VEPs) in patients with chronic IIH, as a non-invasive tool to detect incipient visual nerve dysfunction. Previously, normal VEP responses were reported in patients with “acute IIH” [4–6], although a few cases had prolonged responses [4]. Another study [7] reported, in a small series of cases, prolonged responses in three eyes of seven patients (one bilaterally), but did not comment on the amplitude of the response. Other reports also included cases with prolonged VEP responses [8–10], but examination of VEP has not usually been recommended in the initial evaluation or follow-up examination of patients with IIH.

2. Methods

We examined 20 consecutive patients with chronic IIH fulfilling the modified Dandy criteria [1]. We excluded patients less than 16 years of age and those with ocular diseases (e.g. uveitis and glaucoma), which could affect visual function or testing. All patients underwent brain computed tomography (CT) with contrast injection and/or magnetic resonance imaging of the brain and veins (MRI and MRV). The neuro-ophthalmological examination included Snellen visual acuity, Humphrey visual field tests and ophthalmoscopic examinations. Disease duration exceeded 6 months in all cases.

VEPs were recorded using Nicolet Viking IV equipment (Madison, WI, USA). The stimulus consisted of a pattern reversal checkerboard of black and white squares sized 30’ and a screen of 11°, changing at a rhythm of 1.9 reversals/s, presented on a display with a luminance of white checks of 80 cd/m², and a contrast of >90%. Two or more sequences of at least 256 trials were averaged for each eye. Responses were recorded from electrode sites Oz, O1 and O2, using Fz as reference, according to the international 10/20 system. Electrode impedance was held below 10 kΩ at all times. Bandpass filter was set at 1–100 Hz. Only one stimulus size (spatial frequency stimulation) is used routinely in our laboratory.
The latency of the P100 peak and the amplitude of the N75-P100 wave were measured. Responses were considered abnormal if absent, if the P100 latencies exceeded 110.85 ms in any eye (mean ± 2.5 SD, according to accepted published data, confirmed and implemented in our laboratory for many years: 98.6 ± 12.25) [11,12], or if the response amplitude was absent (mean – 2.5 SD according to same data: 3.82 ± 2.66). Statistical comparisons were performed using two-tailed t-test, paired or unpaired as required. All procedures were performed according to the Guidelines of the International Society for Clinical Electrophysiology of Vision [13] and the American Clinical Neurophysiology Society [14]. The study was approved by the local institutional research board.

### 3. Results

Twenty consecutive patients (19 females) with chronic IIH were examined (Table 1). Their mean age was 33.3 years (range 16–53 years), mean duration of the symptoms 47.2 months (range 6–240 months). Reduced visual acuity was recorded in five cases (in three bilaterally) while visual fields were abnormal in six cases (in four bilaterally). Optic nerve abnormalities were seen by fundoscopy in 13 cases (all bilaterally).

The mean P100 latency in our patient group was 113.0 ± 13.9 ms (range 81–146 ms). These values are considerably higher than normal values in our laboratory (Chi square p < 0.002). Only nine patients had completely normal VEP response latencies. In most patients, the results were similar for both eyes, except for two patients with significant differences between the eyes (Fig. 1).

Most patients with abnormal fundi (swollen discs or optic atrophy, n > 8) had prolonged P100 latencies (exceeding 110.85 ms). All three patients with bilaterally reduced visual acuity (beyond 8.5 J) had prolonged P100 latency at least in one eye (102, 110, 118, 127, 135 and 146 ms). Visual field defects were observed in six patients, five of who had prolonged P100 latencies at least in one eye (94, 94, 102, 110, 116, 118, 122, 127, 135 and 146 ms).

VEP amplitudes were within normal range in all patients, with a mean value of 6.0 ± 2.9 μV (range 1.8–12.3 μV), without significant differences in patients with normal or prolonged P100 latencies or in those with normal or impaired vision (Table 2).

VEP examinations were repeated 6–12 months after the first tests in five patients with the longest VEP latency (patients 1, 5, 6, 8 and 10 in Table 2). Similar results were obtained in four patients who were clinically stable, while in one patient the VEP latencies improved markedly in parallel to her clinical improvement (Fig. 2).

### 4. Discussion

The pathogenesis of the elevated intracranial pressure in patients with IIH is uncertain. Several mechanisms have been suggested, including increase in the resistance to CSF flow across the arachnoid villi or impaired absorption of CSF leading to elevated cerebral blood volume or an elevated cerebral venous pressure. Others postulate that an abnormality in the cerebral microvasculature is responsible for an elevated cerebral blood volume and that intracranial hypertension in patients with IIH can be explained by tissue swelling from an increase in total water content [15–18].

For unknown reasons, the visual system is particularly sensitive to elevated intracranial pressure. Transient visual obscurations are among the earliest symptoms, while chronic pressure elevation may lead to more significant visual deterioration. Little is known about the mechanism underlying the visual loss, but suspected direct damage to the optic nerves underlies therapeutic fenestration of the nerve [18]. Analogies have been suggested with the visual loss in glaucoma and in acute ischemic optic neuropathy [19–21], where axonal damage occurs in the optic nerves. However, axonal damage should be expressed as low amplitude of the VEP, which indeed is the characteristic finding in the two latter conditions [20,21], but was not observed in our cases. Demyelination of the nerves may be a more likely mechanism, analogous to compression neuropathy in the periphery [22–24], with axonal damage being a late complication. Our results are consistent with this view since they show prolongation of conduction rather than reduction of P100 amplitudes, similar to that seen in multiple sclerosis [25].

We also measured somatosensory evoked responses in four patients, particularly those with the most extreme prolongation of VEP, and found these to be normal. Indeed patients with elevated intracranial pressure do not usually complain of sensory symptoms. They may however complain of dizziness and tinnitus [26] and auditory-evoked responses showed prolonged interpeak latencies in IIH in one study, with improvement after treatment, similarly

![Fig. 1. Correlation between P100 latencies in the right eye and in the left eye with ±2.5 SD (broken lines). The 110.85 ms values are delineated. There is a statistically significant correlation (R = 0.8, p < 0.001) between P100 latencies in both eyes.](image-url)
to the results of VEP in our cases [27]. The special vulnerability of the visual system in IIH has not yet been explained. It is possible to speculate that the demyelination occurs at a specific site, possibly the entrance of the nerve into the cranial cavity.

The incidence of prolonged VEP responses in patients with IIH is debated and depends both on the time point of the examination and the technique used. Verplanck et al. [4] examined VEP responses in 15 women with “acute onset of pseudotumor cerebri”, and found abnormal results in only a small number (5 out of 30 eyes – 17%), while Rizzo et al. [7] and Sorensen et al. [8] found abnormal responses in 28 and 31% of their patients, respectively. Others [5,6], using more elaborated techniques, reported prolonged responses in 55%, and in most of their IIH patients, respectively.

In the present study, we determined a similar frequency of 55% responses in 55%, and in most of their IIH patients, respectively. Our patients had a considerably longer disease history than those included in previous studies, and thus it appears that electrophysiological changes, like the clinical evidence of optic nerve damage, are an expression of a prolonged elevation of the intracranial pressure. The finding of prolonged VEP is not specific for IIH, but was described also in increased intracranial hypertension due to cranial pressure. The finding of prolonged VEP is not specific for IIH, and clinical evidence of optic nerve damage, are an expression of a prolonged elevation of the intracranial pressure. The incidence of prolonged VEP responses in patients with IIH is debated and depends both on the time point of the examination and the technique used. Verplanck et al. [4] examined VEP responses in 15 women with “acute onset of pseudotumor cerebri”, and found abnormal results in only a small number (5 out of 30 eyes – 17%), while Rizzo et al. [7] and Sorensen et al. [8] found abnormal responses in 28 and 31% of their patients, respectively.

Others [5,6], using more elaborated techniques, reported prolonged responses in 55%, and in most of their IIH patients, respectively. In the present study, we determined a similar frequency of 55% prolonged VEP responses in patients with chronic IIH, by use of a simple, not time-consuming routine technique.

Our patients had a considerably longer disease history than those included in previous studies, and thus it appears that electrophysiological changes, like the clinical evidence of optic nerve damage, are an expression of a prolonged elevation of the intracranial pressure. The finding of prolonged VEP is not specific for IIH, but was described also in increased intracranial hypertension due to other causes, as head trauma [28] and craniosynostosis [29]; therefore, reinforcing the assumption that the observed abnormalities are due to a direct influence of the increased intracranial pressure on the optic nerve.

The 20 patients evaluated in the present study are followed up at our neuro-ophthalmology clinic; several of them suffer from the disease for considerable periods, and are under treatment, usually with acetazolamide. It would have been preferable to study a more homogenous group of patients, but this is difficult to achieve. Moreover, even in newly diagnosed cases the duration of the intracranial hypertension is usually unknown.

There was only a poor relationship between the VEP abnormalities and clinical parameters, except that patients with abnormal visual fields tended to have more prolonged VEP latencies. This may suggest that VEP may be a sensitive reflection of damage to the nerves. It remains to be seen whether follow up of VEP parameters can be clinically helpful and replace the need for repeated lumbar punctures.

Acknowledgement

We wish to thank Mr M. Zaretzki, B. Tech., for his exceptional technical assistance.

References