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DIFFERENTIATION OF POSTERIOR ISCHEMIC OPTIC NEUROPATHY FROM RETROBULBAR NEURITIS WITH PATTERN EVOKED VISUAL POTENTIAL RESPONSE

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Summary. *Pattern-evoked responses have been recorded in 21 patients with unilateral retrobulbar neuritis and in 20 patients with posterior ischemic optic neuropathy. In the group of retrobulbar neuritis there were 9 patients with definite multiple sclerosis.*
In posterior ischemic optic neuropathy the P-100 of PVEP was delayed (ave.123.87 msec; normal 106.9 msec), but significant increases in latent period was obtained in the group with retrobulbar neuritis (ave.138.72 msec). One of the most striking differences between ischemic and demyelinating disease of the optic nerve was seen when the normal eye was stimulated. In patients with posterior ischemic optic neuropathy the response was always normal.
In the posterior ischemic optic neuropathy patients, amplitude P-100 of PVEP was reduced more frequently than the latency was increased (ave. 3.97 mV; normal 8.7 mV). Amplitude/latency ratio was also reduced proportionally more than latency was prolonged (0.027 mV/msec ; normal 0.082 mV/msec).
The paper describes pathogenetic mechanisms of ischemia and inflammation and their influence on characteristic PVEP findings in ischaemic neuropathy and optic nerve neuritis.
The conclusion is that PVEP represents a very significant diagnostic method, enabling early differential diagnose in patients with inflammatory and ischemic optic nerve diseases.

Key words: *Posterior ischemic optic neuropathy, retrobulbar neuritis, PVEP*

Introduction

The term optic neuritis is reserved for inflammatory or demyelinating disorders of the optic nerve. There are two forms of optic neuritis, retrobulbar form and papillitis.

Ischemic optic neuropathy may be classified into two types, anterior ischemic optic neuropathy and posterior ischemic optic neuropathy (1,2,3). Retrobulbar neuritis and posterior ischemic optic neuropathy have some similar clinical characteristics and they are in some cases a differential diagnostic problem. In both disorders there are no remarkable changes on the optic disc during the acute stage (4).

The age of the patients (elderly) or presence of the systemic vasculitis or thromboembolic disorder could help in group with posterior ischemic neuropathy, but frequently these parameters are not sufficient for definite differential diagnosis (5,6).

To diagnose and manage optic nerve disease, an ophthalmologist needs quantitative information about optic nerve function. These objective findings include recording of visual evoked potentials during the examination. Visual evoked potentials obtained on pattern stimulation (PVEP) represent an averaged response of the visual cortex induced by repeated visual stimulations and as such reflecting optic nerve function, i.e. its electrophysiologic conductivity of its axons.

To our knowledge, a small number studies have been published defining the visual evoked response findings in differential diagnosis of posterior ischemic optic neuropathy from retrobulbar neuritis (7,8).

Comparing PVEP findings in patients with retrobulbar neuritis and posterior ischemic neuropathy and further comparison with healthy control subjects, we tried to establish specific differences, if any, which would facilitate differential diagnosis of these two diseases.

Material and methods

Twenty one eyes of retrobulbar neuritis and twenty eyes of posterior ischemic optic neuropathy were studied by "pattern" VEP (PVEP). Twenty individuals who were free of disease served as control subjects. All subjects from the control group had visual acuity 1.0 or beter, and patients with retrobulbar neuritis and posterior ischemic optic neuropathy had visual acuity better the 0.1. All groups were examined in the same way. The pattern-reversal stimulation was obtained with the aid of Medelec television pattern generator. The PVEP was obtained using 30-minute black and white checks generated on a television screen subtending 10 degrees of

visual angle horizontally and 19 degrees vertically. The contrast ratio of checks was 98%. Pattern reversal rate was 1 Hz. Responses to 128 pattern reversals were averaged, with the analysis time of 300 msec. The subject were placed 125 cm from the screen. The patients were seated in a semi darkened room (background light intensity of approximately one foot candle). The pupils were not dilated, and corrective lenses were worn.

PVEPs were recorded between an electrode applied to the scalp 5 cm above the union in the midline (Oz) and a midfrontal reference (Fz). Latency was measured to the peak of the major positive P-100 wave, P-100. Amplitude was measured from the peak of the preceding negative wave to the peak of this positive wave. Data were analyzed using Student's t -test.

Results

There were 21 patients with retrobulbar neuritis (9 men and 12 women - average age 34.9 years). In the group with posterior ischemic optic neuropathy there were 20 patients (10 men and 10 women - average age 53.8 years).

In the reference group the mean PVEP latency for the first negative peak (P-100) was 106.9msec (SD ±5), and interocular difference was less than 7msec. The mean PVEP amplitude was 8.7±1,4mV. Table 1 presents the pattern VEP data in the different groups.

Table 1. Mean and SD of the PVEP in the different groups

Groups	PVEP		
	Lat (ms)	Amp (mV)	Amp/Lat
Control	106.0 ± 5	8.7 ± 1.4	0.082 ± 0.02
RN group	136.5 ± 9	6.7 ± 2.9	0.050 ± 0.04
PION group	124.4 ± 6	3.9 ± 3.5	0.027 ± 0.09

The group with retrobulbar neuritis (RN) had significant prolongation of the PVEP latency (mean: 136.5±9 ms), and moderate decrease of amplitude (mean: 6.7±2,9 mV), and amplitude/latency ratio (mean: 0.050±0,02 mV/ms). Results in posterior ischemic optic neuropathy (PION) patients showed a mild increase of the PVEP latency (mean: 124.4±6 ms), and high degree of amplitude decrease (mean: 3.9±3,5 mV) and amplitude/latency ratio (mean: 0.027±0.09 mV/ms).

The mean values of PVEP abnormalities, and it statistic correlation is shown in Table 2.

Table 2. VEP abnormalities in retrobulbar neuritis and posterior ischemic optic neuropathy

TEST	RB	PION	p
VEP amplitude	6.7 mV	3.9 mV	< 0.001
VEP latency	136.6 ms	124.4 ms	< 0.05
A/L ratio	0.050	0.027	< 0.01

The group with posterior ischemic optic neuropathy had significantly reduced amplitude ($p<0.001$) and amplitude/latency ratio compared with group with retrobulbar neuritis ($p<0.01$).

Both groups, the patients with retrobulbar neuritis and the patients with posterior ischemic optic neuropathy, had an abnormally prolonged latency of PVEP, but the group with retrobulbar neuritis had significantly longer mean latency than mean latency change in patients with PION ($p<0.05$).

In 6 of 9 patients with retrobulbar neuritis caused by multiple sclerosis the VEP response of the second eye was abnormal, with prolonged latency of the major positive component. When the normal eye was stimulated in patients with posterior ischemic optic neuropathy, the response was always normal. The mean response obtained by stimulating the unaffected eye in the group with retrobulbar neuritis caused by multiple sclerosis showed a significant prolongation of P-100 latency ($p<0.01$) (Table 3).

Table 3. PVEP finding in the unaffected eye of a patient with retrobulbar neuritis and posterior ischemic neuropathy

Groups	PVEP – P/100		
	mV	ms	mV/ms
RB group caused by MS	7.14	121	0.06
RB group without MS	11.2	105.1	0.1
PION group	10.8	103.3	0.12
P(t-test)	> 0.05	< 0.01	< 0.05

Discussion

Visual evoked potentials are an electrophysiological method used routinely nowadays in diagnosis of various optic nerve afflictions. Throughout the literature there are numerous reports on VEP findings in patients with optic nerve neuritis (1,9,10). On the other hand, posterior ischemic neuropathy belongs to the clinical entities insufficiently evaluated regarding clear clinical picture and diagnostic options. In view of the polymorphic findings in posterior ischemic neuropathy and clinical and ophthalmologic features, the disease was often erroneously classified as neuritis. A special differential diagnostic problem may occur in middle aged patients (40-50) in which there may exist an equal frequency of inflammatory and vascular optic nerve diseases (2,8).

Due to the fact that the ophthalmologic pictures in both retrobulbar neuritis and posterior ischemic neuropathy is not of much use, any accessory method enabling early diagnosis is of great significance. Visual evoked potentials may therefore have a crucial role in diagnostic proceedings, especially for cases with more pronounced reduction of sight acuity, where we cannot obtain characteristic findings with primetry, assessment of color sight and other diagnostic methods (4).

In 21 patients with retrobulbar neuritis a high increase of the latent period for the major positive wave PVEP was noted. We found VEP latency changes to be more prominent in retrobulbar neuritis than in posterior ischemic optic neuropathy. Other investigators have had similar results when they compared the patients with optic neuritis and anterior ischemic optic neuropathy (8,10).

The typical VEP in 20 patients with PION had noticeably reduced amplitude and amplitude/latency ratio with mildly prolonged latency. However, a VEP latency delay of 30 msec or more supports a diagnosis of retrobulbar neuritis over PION (9).

What are the factors influencing a significant P-100 wave prolongation on PVEP in patients with retrobulbar neuritis and significant amplitude and A/L index reductions in cases of posterior ischemic neuropathy (which in a way are essential electrophysiological features of these diseases)?

Above all, in order to properly interpret these findings one should know basic pathogenetic mechanisms in inflammatory and ischemic optic nerve diseases. Inflammatory mechanisms inducing retrobulbar neuritis create in fact inflammation foci, and the disturbed conduction of electric impulses through the axons can be the consequence of a damaged axon itself or damaged axonal myelin sheath (2,11).

In cases of inflammation and demyelinisation, depending on the level of damage, there occurs significantly slowed down axonal transmission, with prolonged P-100 wave latency and amplitude reduction proportional to the visual acuity reduction.

The next table presents PVEP findings in a patient with retrobulbar left eye neuritis, with apparent prolongation of P-100 wave latency and mild amplitude reduction.

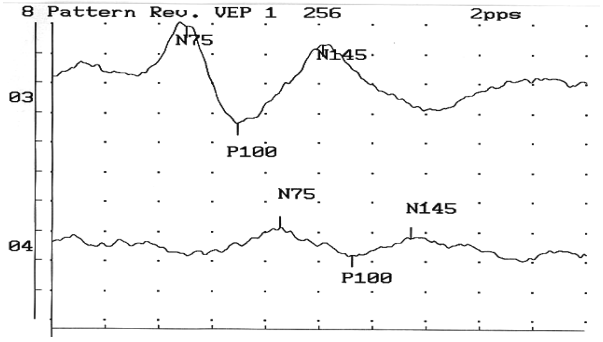

Fig. 1. PVEP finding in retrobulbar left eye neuritis, with normal right eye values

With the recovery of visual function (occurring relatively quickly in retrobulbar neuritis), PVEP wave amplitudes almost reach normal values, while latency remains prolonged due to slowed down conduction through the demyelinated axons.

In posterior ischemic neuropathy ischemic damage of the posterior parts of optic nerve occurs as the result of obstruction of its vascular network. Ischemia damages optic nerve axons in a much more serious way, with a number of them permanently damaged and a number in ischemic state with possible recovery (2,12).

The third group of axons is generally spared of ischemic lesions. We may expect this to happen in cases of mild or moderate ischemia, while in more severe cases intensive ischemia may occur inducing permanent ischemic damage of a significant number of optic nerve axons (associated with a marked visual acuity reduction and overall poor prognosis).

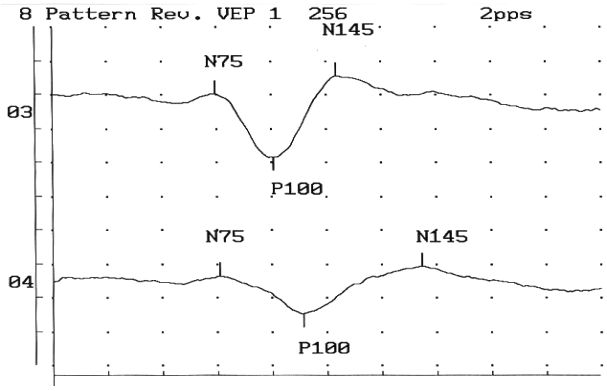

Fig. 2. PVEP findings in the left eye of a patient with posterior ischemic neuropathy and normal right eye findings

In our patients visual acuity of the affected eye was above 0.1, which indicates that a number of axons of the optic nerve was spared of ischemia at the time of study.

In our patients visual acuity of the affected eye was over 0.1, which suggests that a number of axons of the optic nerve was spared of ischemia.

PVEP findings in patients with posterior ischemic neuropathy may be explained with these pathogenetic mechanisms; in these cases prominent are amplitude reduction and P-100 wave latency prolongation, though less than in cases of bulbar neuritis. It is thought that the conductivity through the preserved axons is unaffected and thus we have a lesser prolongation of latency response compared to optic nerve neuritis. Amplitude reduction is also associated with the degree of visual acuity reduction, but due to worse prognosis of ischemic neuropathy it generally remains as a permanent feature.

One of the most striking differences between posterior ischemic optic neuropathy and retrobulbar neuritis caused by multiple sclerosis was seen when the normal eye was stimulated. In patients with posterior ischemic optic neuropathy the response was always normal.

Pathologic findings in the contralateral, unaffected eye is a common and very important diagnostic sign in patients with retrobulbar neuritis caused by demyelinating disorders. It is well known that in some cases multiple sclerosis manifests itself by retrobulbar neuritis as a first sign of the disease. In such cases we encounter visual acuity reduction in the affected eye associated with the characteristic PVEP finding (most frequently prolonged P-100 wave latency.

In a significant number of cases due to the demyelization focus on the other optic nerve without clinical evidence, with VEP we may register disturbed conductivity, though in a lesser degree. On the contrary, in patients with retrobulbar neuritis of some other etiology as well as in patients with ischemic neuropathy we most commonly have normal PVEP findings since those are unilateral diseases (6,13).

We conclude that the PVEP provides a useful diagnostic and monitoring tool for patients with posterior ischemic optic neuropathy and retrobulbar neuritis. Thus PVEP recording is highly recommended in evaluation of posterior visual pathway disorders.

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DIFERENCIJALNA DIJAGNOZA ZADNJE ISHEMIČNE NEUROPATIJE I RETROBULBARNOG NEURITISA UZ PRIMENU VIZUELNIH EVOCIRANIH POTENCIJALA

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Kratak sadržaj: *Strukturni vizuelni evocirani potencijali (PVEP) su registrovani kod 21 pacijenta sa unulateralnim retrobulbarnim neuritisom i kod 20 pacijenata sa zadnjom ishemičnom optičkom neuropatijom. U grupi sa retrobulbarnim neuritisom bilo je devet pacijenata sa klinički potvrđenom multiplom sklerozom.*

Kod pacijenata sa zadnjom ishemičnom neuropatijom vrednosti P-100 talasa PVEP-a bile su produžene (123,87 msec; normalno 106,9 msec), ali signifikantno produženje latentnog vremena je bilo prisutno u grupi sa retrobulbarnim neuritisom

(138,72 msec). Jedna od najznačajnijih razlika između ishemične i demijelinizirajuće bolesti vidnog živca je registrovana u slučaju kada je zabeležen odgovor zdravog oka. Kod pacijenata sa zadnjom ishemičnom neuropatijom ovaj odgovor je bio uvek normalan.

Kod pacijenata sa zadnjom ishemičnom neuropatijom aplitude P-100 talasa su bilo znatno više reducirane u odnosu na produženje latence (3,97mV; normalno 8,7mV). Indeks amplituda/ latenca je u ovoj grupi je takođe bio značajno izmenjen u odnosu na produženje latence (0,027mV/msec; normalno 0,082 mV/msec).

U radu se govori o patogenetskim mehanizmima ishemije i inflamacije i njihov uticaj na karakteristike na nalaz PVEP-a, kod ishemične neuropatije i neuritisa vidnog živca.

Zaključuje se da strukturni vizuelni evocirani potencijali predstavljaju vrlo značajanu dijagnostičku metodu, koja nam omogućuje ranu diferencijalnu dijagnozu kod pacijenata sa inflamatornim i ishemičnim obolenjima vidnog živca.

Ključne reči: *Zadnja ishemična neuropatija optikusa, neuritis retrobulbaris, PVEP*