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Retrospective analysis of pattern VEP results in different ocular and systemic diseases

Retrospektywna analiza wzrokowych potencjałów wywołanych w przypadkach istnienia różnych chorób układowych i chorób oczu

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Summary: Purpose: Significantly increased latency of VEP assessment in various ocular and systemic disorders and discussion of VEP interpretation problems in patients with sudden loss of visual acuity.
Material and methods: A retrospective analysis of pattern VEP in 352 patients with suspected retrobulbar optic neuritis and 892 patients with significantly increased (more than three standard deviations) P100 latency was performed. Transient pattern VEP (PVEP) was recorded in accordance with ISCEV standards with the use of two active electrodes in the occipital region (from left and right sides).
Results: The most frequent cause of increased P100 latency was multiple sclerosis. Other conditions associated with delay P100 latency included: macular dystrophies and degenerations, optic neuritis, glaucoma and other optic neuropathies, circulatory problems, chorioretinitis, arterial hypertension, diabetes, ischemic heart disease, chronic renal failure, acute pancreatitis, pediatric problems, and initial cataract. Sudden loss of visual acuity was caused by: retrobulbar optic neuritis (50%), anterior ischemic optic neuropathy, spasm of accommodation, migraine and functional disorders.
Conclusions: If VEP results are normal, visual acuity loss is usually functional. A detailed knowledge of all the factors, which may influence VEP, is essential for its correct interpretation.

Słowa kluczowe: wzrokowe potencjały wywołane, czas reakcji, zapalenie nerwu wzrokowego, upośledzony wzrok, stwardnienie rozsiane, niedowidzenie.

Key words: visual evoked potential, reaction time, optic neuritis, low vision, multiple sclerosis, amblyopia.

Introduction

Optic neuritis (ON) is the most common cause of sudden loss of visual acuity with no ocular abnormalities. Most of optic neuritis cases are an ocular manifestation of systemic disease, namely multiple sclerosis (MS). A proper diagnosis of ON is important not only for treatment, but also in long-term prognosis for the patient. The best way to check the function of optic nerve is assessment of visual evoked potentials (VEP). The changes of VEP peak latency and amplitude reflect functional abnormalities of optic nerve and visual pathways. This changes are correlated with degree of impairment. It is helpful in monitoring progression of diseases. Increased P100 latency is caused by neuronal transmission impairment. Loss of myelin sheath and swelling or compression of the optic nerve are the most common causes. Apart from optic nerve diseases, other ocular or systemic pathologies may interfere with VEP result and sometimes significantly delay VEP latency may occur in patients without ON or MS. On the other hand, normal VEP with no signs of ON (normal peak latency, amplitude and waveform) should initiate search of other reasons of low visual acuity (first of all functional) and prevent from steroid therapy introduction.

Normal ranges of VEP P100 amplitude and latency are determined individually by each laboratory and should include age and type of stimulation. Non-pathological factors should also be considered in interpretation. Pattern VEP P100 wave amplitude is lower in case of uncompensated refractive errors, poor fixation and lack of attention, increased muscular tension, poor general condition of the patient. Latency is more stable. In identical conditions of stimulation and proper age group, only minor differences in latency between sexes were reported (shorter latency in women) (1,2).

It is difficult for neurologist to interpret VEP amplitude without ophthalmologic examination. Neuroophthalmologists may also have problems with proper diagnosis in patients with several comorbidities known to affect VEP results. The main aim of clinical electrophysiology is to assess the cause of low vision, diagnostic approach and treatment options in patients, whose clinical assessment is insufficient. During 18 years of electrophysiological examinations, I have encountered many interpretation difficulties, arising from imperfections of electrophysiological methods, but also I have corrected many inaccurate diagnoses based on sole clinical examination. They have mainly concerned functional vi-

sion disorders assumed to be ON or cases optic neuritis identified as simulated or congenital amblyopia.

Aims of the study

1. To identify the diseases, in which VEP latency may be significantly prolonged.
2. To present the reasons of sudden loss of vision, in which VEP latency is normal or increased.

Patients and methods

A retrospective analysis of pattern VEP in patients with sudden loss of visual acuity suspected due to retrobulbar optic neuritis (352 patients), and all cases of significant delay (over three standard deviations) of P100 latency (892 patients) was performed. Some patients with sudden decrease of visual acuity and increased VEP latency were also included in the group of patients with increased latency. A group of patients with good compliance and confirmed clinical diagnosis in additional examinations (laboratory tests, imaging etc.), which were consulted by various specialists (ophthalmologist, neurologist, neurosurgeon, internist, endocrinologist, pediatrician, or radiologist) as needed, was selected out of several thousand patients assessed in electrophysiology lab (of the Ophthalmology Department, from 1991 until 2007), and included in the analysis. In the analysis of changes in course of systemic diseases only patients without co-morbidities (namely with arterial hypertension alone or diabetes alone or hyperthyreosis alone), were selected.

Transient pattern VEP was recorded using equipment by LKC (USA), EPIC-4 (1991-1997) and UTAS E-2000 (1997-2007) software in accordance with ISCEV standards (3), but using two active electrodes in the occipital region (left- and right-sided) and 1.9 Hz pattern frequency. Four pattern element sizes were used (105', 52', 26', and 13' checkerboards). P100 latency had to be increased after all stimulations to include patient to analyzed group. The reversal rate was 1.9 Hz. The results from 954 patients in age between 2 and 88 (mean 47 years), were compared with my own normal values in relation to age groups (following age groups were regarded: 2-12; 13-19; 20-49; 50-59; 60-69; >70). In normal subject differences of P100 latency between right and left eye and between right and left brain hemisphere are less than 3 ms.

Results

A total number of examined eyes was 1908. In this group, I found normal pattern VEP in 261 (14%) eyes, significant delay in 1.632 (85%) eyes and unrecordable in 15 (1%) eyes. The reasons for significant increase of P100 latency are presented in Table I.

Toxic optic neuropathies were caused by acute intoxication with various toxins (tobacco-alcohol amblyopia – 11 patients, tranquilizers overdose – 3 patients), or by chronic intoxication with lead (14 patients) or medicines (12 patients). This group also included patients with chronic renal failure (5 patients).

In the group of patients with sudden visual acuity loss, normal PVEP was found in 62 persons and abnormal in 290 cases. The reasons for sudden visual acuity loss in patients with normal VEP are presented in Table II, and with increase VEP in Table III.

Optic neuritis was most prevalent in young people (mean age 32 years), and seldom found in children. Out of 175 patients with optic neuritis, only 5 (3%) were below 13 years old. In most cases, optic neuritis affected only one eye at a time. Bilateral optic neuritis was diagnosed in about 10% of patients.

Ischemic optic neuropathies (AION, diabetes, systemic hypertension, ischemic heart disease)/ Niedokrwienna neuropatia nerwu wzrokowego (AION, cukrzyca, nadciśnienie tętnicze, niedokrwienne choroby serca)	**99**	**6**
Non-SM optic neuritis	90	5.5
Toxic optic neuropathies	90	5.5
Optic atrophy	78	4.8
Ophthalmopathy in Graves' disease	73	4.5
Retinitis, chorioretinitis, neuroretinitis	73	4.5
Brain circulatory problems or stroke	52	3.2
Brain tumor	52	3.2
Retinal degeneration and high myopia	42	2.6
Amblyopia	42	2.6
Head trauma	32	2
Congenital nystagmus	30	1.8
Infantile paralysis	24	1.5
Retinal vessels thrombosis, spasm, embolism	19	1
Tumor of orbit	19	1
Infantile encephalopathy due to hypoxia	10	0.6
Immaturity of the macula	8	0.5
Total	1632	100

Tab. I. Main diseases in which significantly increased P100 latency was noted.
Tab. I. Najważniejsze choroby, w przebiegu których znacząco wzrósł okres utajenia P100.

Diagnosis/ Diagnoza	**Number of patients/ Liczba pacjentów**
Malingering	21
Problems with refraction and accomodation	20
Histery	6
Deep personality disorders	5
Depression	4
Stress induced visual acuity loss	4
Migraine with abnormal pupillary reactions	2
Total	62

Tab. II. Reasons of sudden visual acuity loss in patients with normal VEP.
Tab. II. Przyczyny nagłej utraty ostrości wzroku u pacjentów z normalnymi WPW.

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Diagnosis/ Diagnoza	Number of patients/ Liczba pacjentów
Optic neuritis (SM or non-SM)	175
Retinitis or neuroretinitis	35
Anterior ischemic optic neuropathy	33
Brain tumor	20
Thrombosis or embolism of retinal vessels	19
Central serous retinopathy	8
Total	290

Tab. III. Reasons of sudden visual acuity loss in patients with increased P100 latency of VEP.
Tab. III. Przyczyny nagłej utraty widzenia u pacjentów z przedłużoną latencją P100 w WPW.

Changes in VEP, which were very similar to those found in optic neuritis, were also observed in inflammation or degeneration of the macula, in orbital, eye and sometimes brain tumors (especially chiasmal tumors) and in amblyopia. VEP abnormalities in several common diseases with similar VEP recording are shown in Figure 1.

The most difficult diagnostic problem was recurrent acute retrobulbar optic neuritis in MS patients with optic atrophy and VEP with very low amplitude and increase of latency even during remission. In these patients, false positive (2 eyes) and false negative (1 eye) diagnoses were made.

Discussion

Increase of P100 latency in ON is a well known phenomenon and was described not only during the acute stages of the disease, but also later on (4-8). In some papers, authors reported, that latency was more increased in ON than in ischemic optic neuropathy (9) or macular diseases (10,11). The significantly increased latency in course of ON in MS patients was found also in clinically unaffected eyes (12). In most cases of optic neuritis, only one eye at a time is affected. Thus, interocular amplitude and peak latency analysis are very important in diagnosis of present neuritis, especially because amplitude and waveform of the response from each eye of a given individual is very similar (2). Bee and co-workers described 5 bilateral ON among 22 patients (13) and Frederiksen and co-workers 10 out of 48 (12), what makes 23% and 21%, respectively. In our larger group of patients (175 patients), prevalence of bilateral ON was about 10% (18 patients). The most difficult diagnostic problem is recurrent acute retrobulbar optic neuritis in MS patients with optic atrophy and very low and increased VEP even during remission. If a patient with poor vision complains of vision deteriorating, and VEP responses are flat with peaks covered with noise for a long time, even comparison with previous VEP recording may be insufficient to make proper diagnosis. In these patients, false positive and false negative diagnoses were occasionally made.

All patients with functional problems had bilateral visual acuity loss and normal VEP. This is worth emphasizing, and should be taken under consideration in establishing diagnosis of ON.

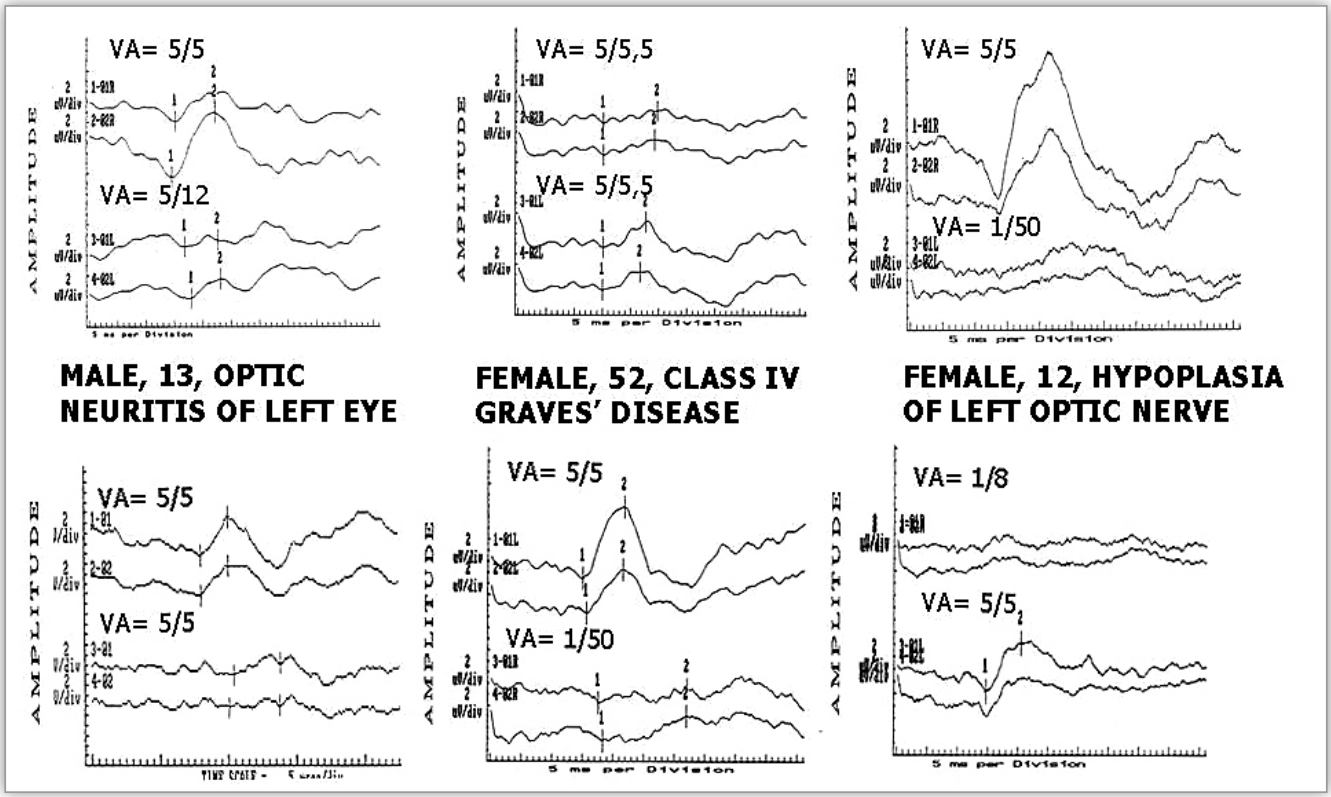

Fig. 1. Pattern VEP in some common diseases with similar VEP picture. Stimulation size 26 min of arc. R – right eye, L – left eye, 01 – left brain hemisphere, 02 – right brain hemisphere, VA – best corrected visual acuity, 13 – 13-years old, 52 – 52-years old, etc.
Ryc. 1. WPW w przebiegu niektórych chorób ogólnych z podobnym zapisem WPW. Wielkość bodźca – 26 minut kątowych. R – prawe oko, L – lewe oko, 01 – lewa półkula mózgu, 02 – prawa półkula mózgu, VA – najlepiej skorygowana ostrość wzroku. 13 – 13-letni, 52 – 52-letni, itp.

On the other hand, significantly increased P100 latency was also found in patients taking potent psychotropic or sedative drugs. These patients sometimes suffer from various visual problems or low vision and are suspected of ON. Gotz-Wieckowska and co-workers used VEP for discrimination between functional and organic diseases in children and young people with visual problems. Normal VEP were obtained from all patients with psychological disorders (14). Electrophysiological signs resembling ON were also described in patients with brain tumors (15-18). Delayed VEP in optic atrophy occurred especially when atrophy was secondary to an inflammation or ischemia (patients with atherosclerosis) (19) and also in hereditary diseases (20-22). Sobolewski and Stankiewicz (19) did not find delayed VEP in toxic atrophy. In my patients, delayed VEP was most common in chronic intoxication, especially in chronic environmental lead intoxication (28 eyes from 14 patients) without any other clinical signs of optic neuropathy (23). Lead probably causes optic nerve demyelinisation and the observed VEP changes are MS-like. Before a diagnosis of MS is made, one should check for history of migration away from the polluted environment, where the patient had lived for a long time.

Numerous authors found delayed VEP in glaucoma (24-29), diabetes (30-35) and amblyopia (36-38). In amblyopia, increased latency was observed in both amblyopic and normal eye, but the latency was significantly higher in amblyopic eyes (38). An experimental systemic hypertension in rats increased latency of flash VEP (39). Tandom and Ram found increased latency in 26% of patients with isolated primary hypertension (40). Increased latency was also found in patients with brain stroke (41) or after a trauma (42), and in children with infantile cerebral palsy (43).

I recommend using two active electrodes on the left and right side. This mode of VEP recording gives more information about pre- or postchiasmal brain lesions and is useful for the diagnosis.

Conclusions

If VEP results are normal, visual acuity loss is usually functional. A detailed knowledge of all factors, which may influence VEP, is essential for correct interpretation.

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