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Wzrokowe potencjały wywołane wzorcem we wczesnej diagnostyce neuropatii nerwu wzrokowego w przebiegu oftalmopatii Gravesa

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Streszczenie

Wstęp: Celem pracy była identyfikacja wczesnych objawów neuropatii nerwu wzrokowego u pacjentów z oftalmopatią Gravesa (GO, *Graves' opthalmopathy*) bez objawów klinicznych neuropatii przy zastosowaniu wzrokowych potencjałów wywołanych wzorcem (PVEP, *pattern visual evoked potentials*) i porównanie wartości pomiarów PVEP (latencje P100 i N75, amplituda P100) z ciśnieniem śródgałkowym i stopniem wytrzeszczu.

Materiał i metody: U 15 pacjentów z GO bez klinicznych objawów neuropatii nerwu wzrokowego i 12 zdrowych osobników badano współzależności między latencjami N75 i P100 oraz amplitudą P100, a pomiarami ciśnienia śródgałkowego i stopniem wytrzeszczu.

Wyniki: Średnie wartości pomiarów latencji N75 i P100 w grupie pacjentów z GO były istotnie dłuższe w porównaniu z kontrolą (LP100–106,2 ± 4,4 ms *vs.* 102,4 ± 2,7 ms; $p < 0,01$ i LN75–79,0 ± 3,7 ms *vs.* 73,9 ± 2,8 ms; $p < 0,001$). U chorych z GO obserwowano pozytywną korelację między latencją N75 a stopniem wytrzeszczu ($R = 0,51$; $p < 0,01$). Wartości LP100 i LN75 były wydłużone ponad normę w 5 na 30 oczu (17%) i w 3 na 30 (10%).

Wnioski: Pomiary wzrokowych potencjałów wywołanych wzorcem (szczególnie latencją P100) u pacjentów z GO bez jawnych objawów neuropatii jest przydatnym narzędziem we wczesnej diagnostyce neuropatii nerwu wzrokowego.

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Słowa kluczowe: *subkliniczna neuropatia nerwu wzrokowego, oftalmopatia Gravesa, wzrokowe potencjały wywołane wzorcem*

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Pattern visual evoked potentials in the early diagnosis of optic neuropathy in the course of Graves' ophthalmopathy

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Abstract

The aim of the study: to investigate by means of pattern visual evoked potentials (PVEPs) early neuropathic changes in Graves' ophthalmopathy (GO) patients without any clinical symptoms of optic neuropathy in order to evaluate the prevalence of subclinical optic neuropathy in GO patients and to elucidate whether there is a relationship between PVEP (P100 and N75 latency), intraocular pressure (IOP) and exophthalmometry.

Material and methods. Two groups of patients were examined: 15 patients with GO without clinical signs of dysthyroid optic neuropathy (DON) and 12 healthy controls. The correlations between the N75 and P100 latencies, IOP and Hertel exophthalmometry were investigated.

Results. The mean PVEP N75 and P100 latencies were significantly delayed in the GO uncomplicated with DON in comparison with controls (LP100- 106.2 ± 4.4 ms vs. 102.4 ± ± 2.7 ms, $p < 0.01$ and LN75- 79.0 ± 3.7 ms vs. 73.9 ± 2.8 ms, $p < 0.001$). In GO patients we documented a positive correlation between the LN75 latency and exophthalmometric readings ($R = 0.51$; $p < 0.01$). The value of LP100 and LN75 was above the normal limit in 5/30 eyes (17%) and in 3/30 eyes (10%) respectively.

Conclusions: The assessment of PVEPs (especially the P100 latency) in GO patients without clinical signs of DON is a useful tool for the early diagnosis of optic nerve involvement.

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Key words: *subclinical optic neuropathy, Graves' ophthalmopathy, pattern visual evoked potentials*

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Introduction

Graves' ophthalmopathy (GO) is a complex autoimmune reaction to orbital structures that results in a variety of ophthalmological symptoms and signs [1]. Dysthyroid optic neuropathy (DON), although infrequent, is one of the most serious complications of GO. It develops in approximately 5–10 % of patients with GO [2, 3]. It is commonly recognised that DON is due to increased muscle volume exerting pressure on the optic nerve and its blood supply at the orbital apex [1, 4–6]. The optic neuropathy may develop without exophthalmos or any sign of GO [3]. Clinical symptoms of DON such as decreased visual acuity, relative afferent defect, oedema of the optic nerve head, visual field defects and colour vision impairments are neither invariably present nor specific for diagnosis [2–4]. Diagnosis of DON at the subclinical stage may be crucial in so far as the visual field loss is not irreversible.

Pattern visual evoked potentials (PVEPs) are the most sensitive indicator of incipient optic neuropathy. The use of PVEPs has been proved useful for the diagnosis of optic nerve impairment in GO [7–11].

In the present study a PVEP investigation was performed of early changes in patients with GO without any clinical symptoms of optic neuropathy to evaluate the prevalence of subclinical optic neuropathy in GO patients and to elucidate whether there is a relationship between the PVEP dominant components (P100 and N75 values) and intraocular pressure (IOP) and exophthalmometry.

Material and methods

The study was carried out on 27 individuals: 15 patients (30 eyes) with Graves' disease and with symptoms of GO, including proptosis, extraocular muscle dysfunction or/and periorbital oedema and 12 healthy volun-

teers (24 eyes). The GO group of patients consisted of 3 men and 12 women with a mean age of 35.6 ± 11.3 years. All GO patients had been euthyroid for at least three months before the examination without any clinical or perimetrical signs of evident optic neuropathy. All of them had experienced a first episode of GO with a clinical activity score of 2 to 5. None of them had diabetes or hypertension. Five (three women and two men) were smokers. A total of 12 healthy volunteers were age and sex matched to serve as the control group (two men and ten women with a mean age of 28.6±11.2). In the group under investigation four patients had diplopia, three revealed ocular motility impairment, one had convergent strabismus and one did not have stereopsia. In addition two subjects had other ocular symptoms (two had positive Moebius and one Kocher symptoms). Patients who had one or more of the following symptoms were excluded from the study: a decrease in best corrected visual acuity, failure in the Ishihara colour test, a relative afferent papillary defect, oedema of the optic nerve head or a field defect. Other exclusion criteria were previous orbital radiotherapy or surgical decompression, severe myopia, astigmatism, cataract or glaucoma.

All the patients underwent a complete ophthalmic examination including best corrected visual acuity, the Ishihara colour test, biomicroscopic examination of the anterior segment, direct and indirect ophthalmoscopic fundus examination, applanation tonometry and Hertel exophthalmometry and ocular motility. Automated perimetry was performed by a Humphrey visual field analyser, using a threshold strategy (Central 30-2) program. The PVEPs were performed according to the International Standards of the International Society of Clinical Electrophysiology of Vision (ISCEV) (2004 update) [12]. The VEPs were recorded monocularly to reversal of full-field checkerboards. The visual field was 14 and the mean luminance was 70 cd/m^2. The scalp electrodes were placed relative to bony landmarks, according to the international 10/20 system. The anterior/ /posterior midline measurements were based on the distance between the nasion and the inion over the vertex. The active electrode was placed on the scalp over the visual cortex at Oz with the reference electrode at Fz. As ground we used the electrode position at the vertex (Cz). The impedance was less than 5 Khom, the bandpass was 1–100 Hz, the reversal rate was 3 per second and the contrast was 0.70. The stimulated eye fixed a point of reference at the centre of the monitor, while the non-fixated eye was blinded by a patch. The number of sweeps for each eye averaged 80.

Statistical analysis of the N75 and P100 latency and P100 amplitude was performed by the Mann-Whitney U test. The relationship between the N75 and P100 latencies, P100 amplitude, IOP and the Hertel reading was evaluated using the Spearman correlation analysis. The values have been reported as the mean and the standard deviation. A p value of less than 0.05 was considered statistically significant. All data were processed using Statistica 6.0 (StatSoft, Tulsa, OK, U.S.A.).

Results

Table I shows the characteristics of age and sex as well as individual measures of the PVEP P100 and N75 latencies (LP100 and LP75 respectively) and P100 amplitude (AP100), IOP and Hertel values in the groups studied.

The normal limits for the N75 and P100 latencies were estimated as the mean value of the control group ± 3 standard deviations: 82.3 and 110.5 ms respectively. The values of the P100 and N75 latencies were significantly different in the GO group in comparison with the healthy controls (Tab. 2). The exophthalmometry values ranged from 16 to 25 mm and IOP from 10 to 29 mm Hg.

In the GO patients we documented a positive correlation between N75 latency and exophthalmometric readings ($r = 0.51$; $p < 0.01$) (Fig. 1). There was no significant correlation between P100 amplitude or latencies and IOP or Hertel readings.

In the group of patients with GO the value of P100 latency was abnormal in 5 out of 30 eyes (17%) in five patients. In 3 out of 30 eyes (10%) in two GO patients N75 latency was above the normal limit.

Discussion

Visual evoked potentials are the most sensitive indicator of incipient optic neuropathy. Pattern VEPs are more repeatable and can be more precise in the estimation of normal limits than flash evoked visual potentials [7, 8, 12]. Burke et al. suggested that neuropathy selectively affects the high temporal frequency Y-axon, which are numerous in the periphery of the optic nerve and thus more vulnerable to compression [13]. This notion explains functional impairments in the PVEP recordings.

The prolonged P100 and N75 latencies in patients with GO suggest that these values may be used in the diagnosis of functional disorders of the optic nerve. In an early study Neigel et al. reported abnormal PVEPs in 94% of the GO patients with DON but in only 9% of those without DON [4]. More recently Ambrosio et al. have demonstrated that VEPs offer a way of detecting differences between compressive and glaucomatous damage of the optic nerve in patients with GO [11]. He claims that N75-P100 amplitude is a sensitive and very specific indicator in the differential diagnosis. In the present study there was no difference in P100 amplitu-

Table I
The characteristics of age, sex and N75, P100, IOP and Hertel values in the group studied

Tabela I
Charakterystyka grupy badanej: wiek, płeć, N75, P100, ciśnienie śródgałkowe i stopień wytrzeszczu

Patient	Age	Sex	Oz- LN75 [ms]	Oz-AP100 [μV]	Oz- LP100 [ms]	IOP [mm Hg]	Proptosis [mm]	EYE
1	58	M	76.40	4.07	105.5	14	23	L
1			86.53	3.94	99.61	12	22	R
2	50	F	78.65	9.96	103.7	10	21	L
2			76.40	10.51	102.8	12	21	R
3	27	F	78.52	13.42	106.1	18	20	L
3			77.93	15.92	103.7	20	20	R
4	28	F	76.17	12.96	106.1	12	16	L
4			74.71	11.11	107.8	12	15	R
5	26	F	77.93	6.29	101.4	17	19	L
5			75.84	8.39	103.7	17	19	R
6	48	F	78.65	4.76	99.99	15	18	L
6			76.40	5.81	100.8	15	18	R
7	36	F	75.27	3.16	103.1	17	19	L
7			74.41	3.44	103.9	17	18	R
8	23	F	86.13	7.99	110.2	12	21	L
8			80.86	10.69	110.7	14	21	R
9	30	F	81.45	12.79	102.5	16	19	L
9			73.03	10.93	106.1	16	16	R
10	28	F	81.00	5.99	110.2	16	25	L
10			86.00	4.54	99.4	14	25	R
11	23	M	76.40	3.68	106.1	21	21	L
11			76.40	5.7	105.6	21	20	R
12	46	M	77.93	6.37	113.7	16	20	L
12			80.27	8.32	106.1	14	19	R
13	51	F	80.86	2.12	111.3	20	20	L
13			78.65	4.83	106.1	19	19	R
14	34	F	84.38	6.06	107.8	29	23	L
14			86.00	5.82	110.7	26	21	R
15	40	F	77.93	6.21	115.4	14	22	L
15			78.50	4.22	115.4	12	22	R

Table II
The mean values of the evaluated parameters in the group under investigation

Tabela II
Średnie wartości ocenianych parametrów w grupie badanej

	LP100 [ms]	AP100 [μV]	LP75 [ms]	IOP [mm Hg]	Hertel exophthalmometry [mm]
GO	106.2 ± 4.4*	7.3 ± 3.5	79.0 ± 3.7**	mean ± SD 16.3 ± 4.5 range (10–29)	mean ± SD 20 ± 2.6 range (16–25)
Controls		102.4 ± 2.7	6.5 ± 2.5	73.9 ± 2.8	

*p < 0.01 GO vs. controls, **p < 0.001 GO vs. controls

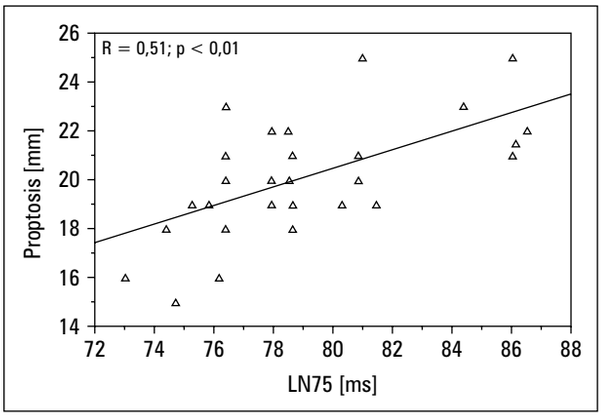

Figure 1. *Correlation between N75 latency and proptosis*
Rycina 1. *Współzależność między N75 a stopniem wytrzeszczu*

de between the evaluated group and the controls. We suggest that this parameter is variable and dependent on many factors.

In the few studies that evaluate the prevalence of asymptomatic optic nerve involvement in GO the percentages of cases are comparable. Most of the authors agree that LP100, as a dominant component of PVEPs, should be evaluated [6–10]. We found that LP100 is a more sensitive indicator of optic neuropathy than LN75. Rutecka-Dębniak et al. noted abnormal P100 latency in 21% (13/62) of the cases with GO without clinically evident optic neuropathy, while Salvi et al. estimated that approximately 23.8% of the cases were with asymptomatic optic nerve involvement [9, 14]. We observed the prolongation of LP100 in 17% (5/30), while LN75 was delayed in 10% (3/30 of the cases) of GO without optic nerve dysfunction. Similarly Rutecka-Dębniak et al. found that prolongation of LN75 occurred less frequently (7.7%–2/26).

Most authors claim that proptosis does not correlate well with DON and may even be protective by expanding the total orbit volume and, in consequence, diminishing the pressure exerted on the optic nerve [1]. In the present study proptosis correlated with a delayed latency of N75. We suggest that this finding reflects an early uncompensated phase of optic nerve dysfunction rather than dysthyroid neuropathy.

Some authors have observed an influence of corticosteroids, radiotherapy and orbital decompression on the PVEP recordings [15]. In the present study, therefore, only patients who had not undergone pharmaceutical or surgical decompression of the optic nerve were included.

Although it is true that CT and standardised echography are helpful for diagnosis of optic neuropathy, they determine the anatomical and not the functional condition of the optic nerve [15]. Sometimes the imaging examinations are not sufficient to detect an early visual deficit. Therefore PVEPs provide a useful diagnostic and monitoring tool in patients with GO, combining objectivity with quantitative analysis.

Conclusions

In conclusion, the assessment of pattern VEPs in GO patients without clinical signs of DON is a useful tool for the early diagnosis of optic nerve involvement. Prolongation of LP100 is, more than that of LN75, a sensitive indicator of incipient optic dysfunction.

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