Graefe's Arch Clin Exp Ophthalmol (1984) 222:29–33

Graefe's Archive
for Clinical and Experimental
Ophthalmology

Pattern electroretinogram and visually evoked cortical potentials in glaucoma

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Abstract. Electroretinograms (P-ERG) and cortical potentials (P-VECP) evoked by checkerboard patterns were examined in patients with defects of the ganglion cell and nerve fiber layers due to glaucoma. Only a few patients exhibited a prolonged latency in the P-VECP, whereas in the P-ERG all patients with papillary and visual field defects revealed a significantly attenuated amplitude. Since there is a substantial fluctuation in the assessment of papillary excavation and visual field, the P-ERG offers a further means of evaluating and follow-up of retinal function in glaucoma patients.

Introduction

The electro-ophthalmological examination of the retina is generally based on the electroretinogram with luminance stimuli. According to Granit (1963) and Miller and Dowling (1970), the retinal components of the response are the activity of the photoreceptors (a-wave) and the extracellular sum potential of the inner nuclear layer (b-wave). Consequently, glaucomatous retinal damage does not result in significant changes in the luminance ERG (e.g., Karpe 1945; G. Leydhecker 1950; Henkes 1951; Schmöger and Zimmer 1965; Bartl 1978; Papst et al. 1984), since changes in the optic disk and the ganglion cell layer dominate.

In addition to the luminance ERG, electroretinograms can also be recorded in response to pattern stimulation (P-ERG). Whereas the luminance ERG, depending on the luminance of the stimulus, produces relatively large amplitudes (up to 400 μV), those of the P-ERG are relatively small (2–4 μV). The origin of this potential has not yet been fully explained, but clinical observations (Groneberg and Teping 1980) and animal experiments (Maffei and Fiorentini 1981, 1982) have established probable correlations with retinal ganglion cell activity. Accordingly, patients with glaucoma-related damage in the area of the ganglion cell layer would be expected to demonstrate an attenuated P-ERG.

Studies of the visual pathways using pattern stimulation have so far been based predominantly on recordings of visually evoked cortical potentials (P-VECP), whereby degenerative, demyelinating, inflammatory, compressive and ischemic lesions in the area of the visual pathways have been detected (Halliday and Mushin 1980; Wilson 1978). In glaucoma patients, changes in amplitude (Ermers et al. 1974; Abe and Iwata 1976; Bartl 1978) and latency period (Abe and Iwata 1976; Bartl 1978; Huber and Wagner 1978; Huber 1981; Sokol et al. 1981; Towle et al. 1983) have been reported.

In the following study, P-ERG findings in 28 glaucomatous eyes are reported and compared with those obtained in the P-VECP.

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Methods

Patients. Twenty-eight eyes affected by primary glaucoma were examined in 15 patients with no other retinal disease, clear optical media, various changes of the optic disk and visual field defects. Each had undergone an Elliot-Fronimopoulos operation at least 1 year earlier (Table 1). Tension was regulated in all patients within a range of 10–22 mm Hg without using miotics. Visual acuity was $\geqq 0.6$. The severity of the diseases was classified according to papillary and visual field findings. For the assessment of papillary excavation three stages were distinguished:

A. Normal papilla
B. Glaucomatous excavation of $\geqq 0.7$ papillary diameter (PD)
C. Glaucomatous optic atrophy with peripheral displacement of the nasal vessels; excavation of 1.0 PD

The visual fields were determined with the Goldmann perimeter (test spots V/4, III/4, I/4, I/2, and I/1). According to a method developed by Aulhorn (1976, 1978), the visual field defects were divided into five groups:

0, normal visual field; I, enlarged blind spot or small paracentral scotomas; II, bjerrum scotoma; III, sectorial quadrantanopia; IV, sectorial multiquadrantanopia.

Stimulation and recording techniques. For the electrophysiological examination, the pattern electroretinogram (P-ERG) and visually evoked cortical potential (P-VECP) recorded in response to contrast-reversal patterns in glaucomatous eyes were compared with those of 30 healthy eyes (15 subjects between 45 and 70 years of age).

The alternating checkerboard pattern was produced on a TV monitor by a Medelec pattern generator and presented monocularly at a distance of 1.5 m with central fixation (each check subtending 50 min of angle, reversing frequency

Table 1. Clinical and electrophysiological data in order of P-ERG amplitude

Patient	Age	Side	Acuity	Papilla	Visual field	P-ERG			P-VECP Latencies	
						Amplitude (μV)	Latencies (ms)		(ms)	
							N	P	N_1	P_2
S.B., ♀	46	L	1.2	A	0	3.71	36	62	86	114
S.B., ♀	46	R	1.2	A	0	3.58	37	62	84	113
S.E., ♀	54	L	1.0	A	0	3.18	40	65	82	117
H.G., ♀	53	R	0.8	A	0	2.85	38	63	83	119
Z.K., ♀	62	L	1.0	A	0	2.80	34	68	75	121
H.R., ♂	74	R	1.0	A	0	2.76	34	68	89	123
L.M., ♀	70	L	0.8	A	0	2.75	35	69	89	116
L.M., ♀	70	R	0.8	A	0	2.70	42	66	87	115
H.G., ♀	53	L	0.8	A	0	2.56	36	62	84	123
S.L., ♀	60	L	0.9	B	II	2.15	34	66	85	118
S.G., ♂	63	L	1.0	B	0–I	2.11	39	66	113	138
W.M., ♀	57	R	1.0	B	I–II	2.00	30	70	87	122
W.M., ♀	57	L	0.6	B	II	1.98	37	62	87	109
S.G., ♂	63	R	1.0	B	0–I	1.89	49	70	106	133
S.E., ♀	54	R	0.7	B	III	1.87	40	64	83	122
K.M., ♂	52	R	0.8	B	II–III	1.86	35	61	104	139
S.G., ♂	70	R	0.6	C	II	1.80	36	64	108	154
R.A., ♂	47	R	0.8	A–B	I	1.59	41	64	102	130
H.R., ♂	74	L	1.0	B	III	1.50	41	65	100	130
Z.K., ♀	62	R	1.0	C	III	1.48	40	62	73	125
E.K., ♂	52	L	0.8	B	II	1.48	36	68	94	134
S.L., ♀	60	R	0.6	C	IV	1.37	34	69	85	116
K.M., ♂	52	L	0.8	C	IV	1.37	42	70	102	133
R.A., ♂	47	L	0.7	A–B	I–II	1.32	39	62	105	131
S.L., ♂	61	L	0.9	B	I	1.30	47	67	102	129
S.L., ♂	61	R	0.6	C	IV	0.92	41	69	124	158
O.J., ♂	73	L	1.0	C	IV	0.68	40	66	112	157
O.J., ♂	73	R	0.8	C	IV	0.59	41	67	121	157

2/s, mean luminance 30 cd/m^2, modulation depth 97%, test field diameter 14.5°). The mean luminance of the examination room was 0.2 cd/m^2.

The P-ERG was recorded between an optically corrected Henkes contact lens and against the ipsilateral earlobe. The P-VECP was determined between one earlobe and an electrode positioned 3 cm above the inion. After amplification and filtering (band width 0.16–32 Hz) the signals were fed into an averager (Nicolet 1170) with artifact suppression (threshold 100 μV) and averaged 256 or 512 times. The processor was triggered by the pattern reversal signal. The digitally stored data were subsequently evaluated.

In the P-ERG the amplitude between the negative and the positive peak as well as the peak latencies were evaluated, and in the P-VECP the latency of the first negativity and the second positivity (P100) were noted. The amplitude of P100 was considered only in the bilateral comparison. Values lying beyond the 2 σ-range were termed pathologic.

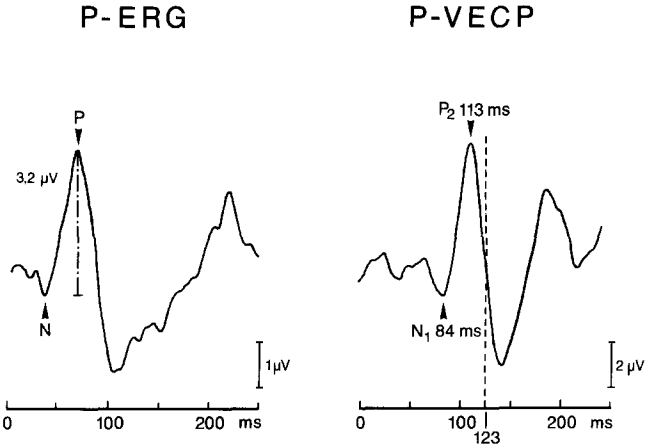

Fig. 1. Original recordings of a typical P-ERG and P-VECP of a 51-year-old man with healthy eyes and an acuity of 1.0. The amplitude in the P-ERG (between N and P) is 3.2 mV and is thus in the normal range; the P_2 latency period in the P-VECP is 113 ms and thus below the marked 2 σ-limit of 123 ms

Results

Normative data

P-ERG. The original curves of a typical P-ERG and P-VECP for a healthy eye with the evaluated parameters are shown in Fig. 1. The values for the 30 healthy eyes yielded a mean value ($\bar{x} \pm 2$ SD) of 36.2 ($\pm$ 6.1) ms for the latency of the negativity and 63.1 ($\pm$6.2) ms for the positivity. For the amplitude the corresponding value was 3.2 ($\pm$0.97) mV. The data obtained agree with those in the literature (Armington et al. 1971; Sokol and Nadler 1979; Persson and Wanger 1982).

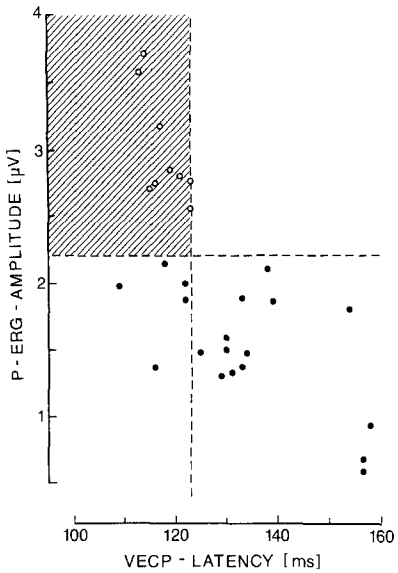

Fig. 2. The normal range ($\bar{x} \pm 2$ s) for the amplitude in the P-ERG and the latency in the P-VECP are *hatched* in the diagram. All patients afflicted with primary glaucoma with normal papillary and visual field findings (o) are within the normal range of P-ERG amplitude and P-VECP latency. Patients with glaucomatous papillary and visual field findings (•) are all below the 2 σ-limit for the amplitude in the P-ERG, whereas latency periods in the P-VECP may be within the normal range of prolonged

P-VECP. The latency values determined from the same group of patients with healthy eyes in the P-VECP yielded a mean value ($\bar{x} \pm 2$ SD) of 84.3 ± 4.9 ms for the first negativity (N_1) and 115.2 (± 7.4) ms for the second positivity (P_2).

Findings in patients

A survey of the clinical and electro-ophthalmological findings from the eyes suffering from primary glaucoma is given in Table 1, comprising a total of 28 eyes of patients aged between 46 and 73 years. As a rule, visual acuity of the affected eye was better than 0.8; in 6 eyes acuity was 0.6–0.7. In 19 eyes glaucomatous papillary excavation was observed with associated impairment of the visual field; the changes were classified according to the stages mentioned above. Figure 2 shows the electro-ophthalmological results obtained in these patients, with the amplitude in the P-ERG (ordinate) plotted against the P_2 latency in the P-VECP (abscissa). As the figure shows, all of the glaucomatous eyes with normal papillary and visual field findings produced normal amplitudes in the P-ERG as well as normal latencies in the P-VECP. By contrast, eyes with glaucomatous papillary changes and associated visual field impairment always displayed normal latencies and reduced amplitudes in the P-ERG. For this group of eyes with glaucomatous damage, both prolonged and normal latency times were found.

A close quantitative correlation between papillary and visual field findings and a decrease in P-ERG amplitude has not yet been established. Although the P-ERG amplitude in patients with visual field defects of stage IV were generally smaller than in those of stage I, no reliable amplitude differences were observed in cases of visual field defects of stages II and III. In the following the characteristic findings are presented in the form of two case reports:

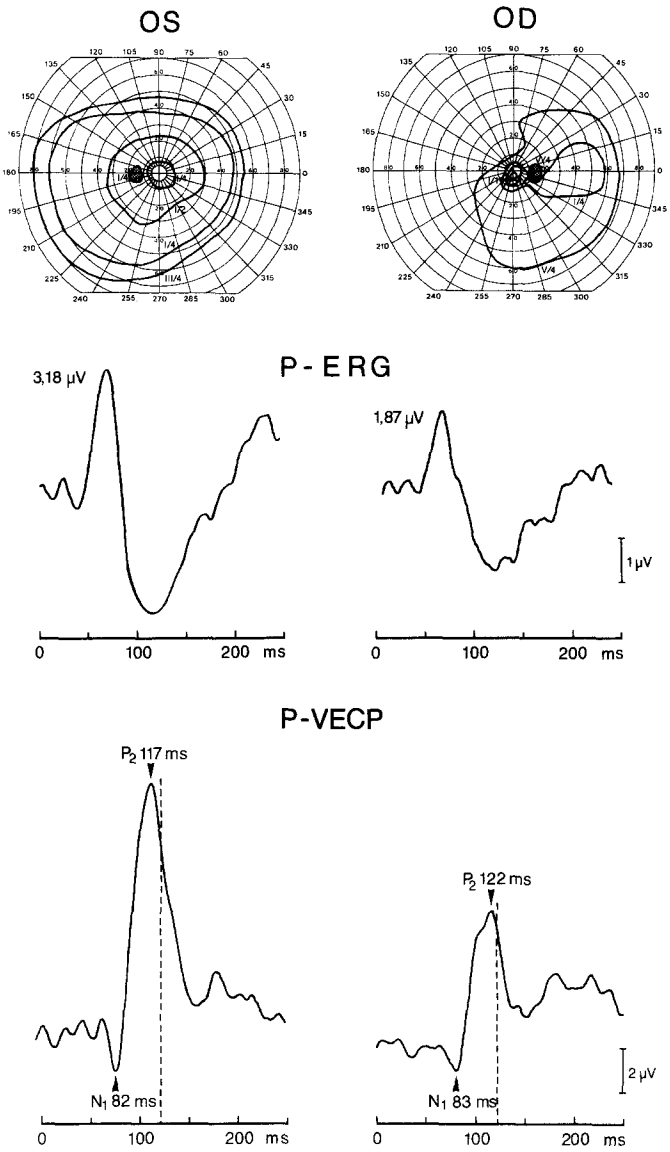

Fig. 3. Visual fields, P-ERG, and P-VECP (original curves) of patient S.E. Unilateral glaucomatous damage of the right eye with an associated unilateral amplitude reduction in the P-ERG. The latency times in the P-VECP are within the normal range for both eyes. Only in the bilateral comparison is an amplitude reduction in the right eye observed

Case 1. Patient S.E. (Fig. 3) revealed pronounced unilateral glaucoma. Whereas the left eye was clinically normal with a visual acuity of 1.0, the right eye had, in addition to a reduction of visual acuity to 0.7, a glaucomatous optical atrophy with papillar excavation of 0.8 PD (stage B) and sectorial visual field losses in one quadrant (stage III). In this patient's P-ERG a decrease in amplitude restricted to the glaucomatous eye was observed, whereas in the P-VECP normal latency was found to be associated with a decrease in amplitude in comparison with the healthy eyes.

Case 2. Patient W.M. (Fig. 4) exhibited bilateral incipient glaucomatous damage to the optic nerve with papillary excavation of 0.7 PD (stage B). While the nonconfluent scotomas (stages I–II) of the right eye were mostly peripheral (outside 20°), visual field losses in the left eye were also found within 10° (stage II). Despite these clinically discrete

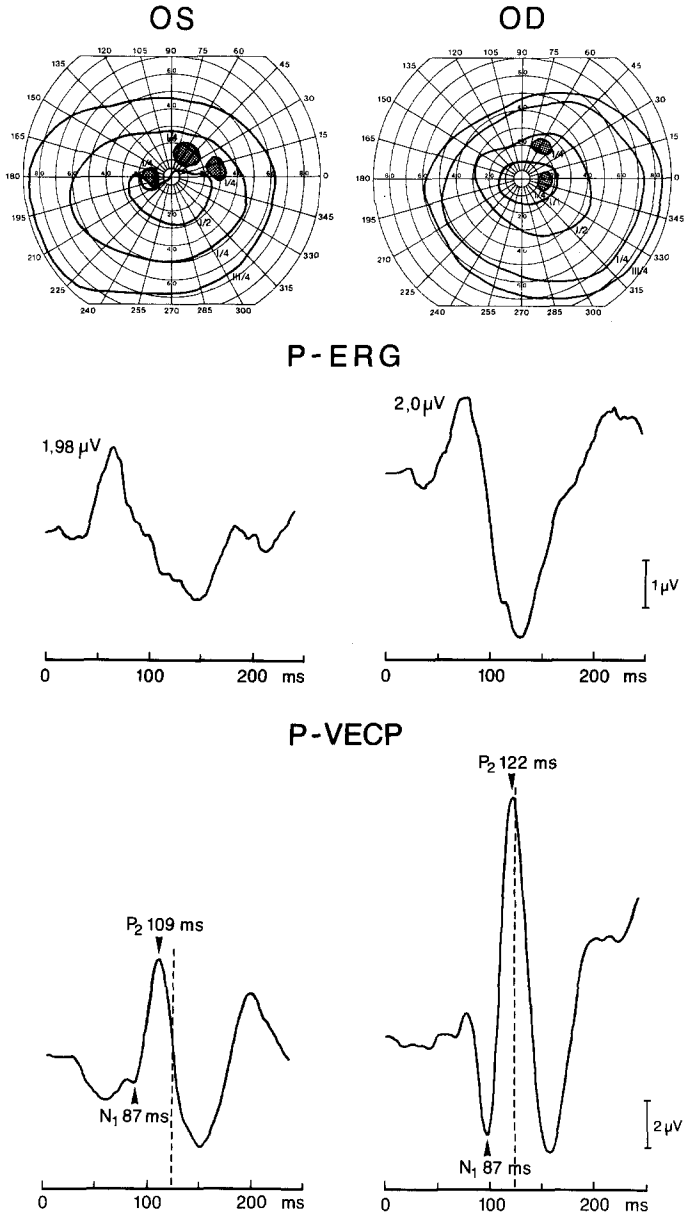

Fig. 4. Visual field, P-ERG, and P-VECP (original curves) of patient W.M. Despite the clinically discrete visual field changes, expecially in the right eye, there were reduced amplitudes in the P-ERG when compared bilaterally. The latency periods in the P-VECP did show a bilateral discrepancy, but both eyes were within the normal range

visual field changes in the right eye, the P-ERG amplitudes were reduced for both eyes. The latencies of the P-VECP for both eyes were within the normal range.

Discussion

The findings for glaucomatous eyes were obtained exclusively from patients whose intraocular pressure had been regulated for a considerable time by a covered fistulating operation and who required no further therapy, in particular no miotics. This was important for an electro-ophthalmologic examination for two reasons: first, pharmacologically induced miosis leads to a prolongation of latency in the P-VECP, even in healthy subjects (Sokol et al. 1981; Hawks and Stow 1981; Penne and Fonda 1981) and, according to our own observations, to a decrease in amplitude in the P-ERG. On the other hand, an increase in ocular pressure above 30 mm Hg causes an amplitude reduction in the P-ERG, which is also observed in cases of clear optical media and unimpaired vision (Papst et al., 1984). Prolonged latencies in the P-VECP have been reported in some patients with elevated intraocular pressure (Bartl 1978; Sokol et al. 1981; Towle et al. 1983).

Like Huber and Wagner (1978) and Towle et al. (1983), we also found prolonged P-VECP latencies in some patients with typical glaucomatous damage. Occasionally a lower amplitude was observed in the P-VECP upon bilateral examination of the more severely damaged eye. On the other hand, all of the patients with typical papillary and visual field changes demonstrated, independent of acuity, a reduction in the P-ERG amplitude to values below the 2 σ-range. The explanation for this probably lies in the cortical representation of the P-VECP, which primarily measures the function of the central retina (Rietveld et al. 1965; Berson 1981; Huber 1981), whereas all stimulated parts of the retina contribute to the P-ERG in different degrees (Groneberg and Teping 1980). Since in the initial stage glaucoma-induced visual field losses are relatively close to the central retina without ever involving it directly (Aulhorn 1976, 1978), parafoveal damage can be better detected by means of the P-ERG than with the P-VECP. Furthermore, the P-VECP amplitude is subject to large intra- and interindividual fluctuations, so that reliable statements on amplitude changes should be based on bilateral comparison.

In histopathological terms, chronic glaucomatous damage is associated with a loss of oligodendrocytes from the myelin sheath and a destruction of retinal ganglion cells (Anderson 1972; Naumann 1980; Quigley et al. 1981). According to Maffei and Fiorentini (1981), section of the optic nerve in cats leads to an attenuation of ERG amplitude or even to the disappearance of pattern-evoked response as a function of the ensuing degeneration of the retina ganglion cells.

In patients with traumatic optic lesions (Groneberg and Teping 1980; Dawson et al. 1982), optic neuritis (Fiorentini et al. 1981; Arden et al. 1982) and central arterial occlusions (Fiorentini 1981) causing a dysfunction of the ganglion cells and their axons, decreased amplitudes in the P-ERG have also been reported. The lowered amplitudes presently observed in the P-ERG of glaucomatous eyes are probably also the expression a functional impairment in the ganglion cell layer of the retina. This is in accordance with observations by Wanger and Persson (1983), who described P-ERG amplitude reductions in unilateral glaucoma in comparison to the opposite, healthy eye.

The reduced amplitudes in the P-ERG observed in visual field losses outside the test field used, as found in the right eye of patient W.M. (Fig. 4), are surprising. The question arises as to whether functional disturbances, which cannot be assessed with kinetic perimetry but can be with static perimetry, might be detectable with the aid of the P-ERG. Since the evaluation of the degree of papillary excavation and the visual field is subject to considerable fluctuation (Leydhecker et al. 1979; Krieglstein 1980; Gramer et al. 1980), the P-ERG, which is sensitive to glaucoma-related damage, lends itself to the detection and follow-up of problem patients, based on reliable *functional* criteria.

Acknowledgements. The authors would like to express their gratitude to Professor E. Dodt for his valuable support of this work,

as well as Mr. D. Hietel for his technical help and Mrs. G. Eckl for her practical assistance.

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Received April 10, 1984