· Brief Report ·

Elecrophysiological tests as an early glaucoma indicator: a cross sectional study

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电生理测试作为早期青光眼诊断指标的横断面研究

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摘要

明视负向反应(PhNR)和图形视网膜电图(PERG)的结果作为评估青光眼的诊断指标。10 例对照组和 15 例早期青光眼患者接受了完整的眼科检查,包括视力测量,眼压(IOP)测量,眼底检查和视野检查。同时进行图形视网膜电图和全视野视网膜点图纪录。青光眼组的平均偏差和图形平均标准偏差显著较低($P<0.001$, $P<0.01$)。PERG N95,PhNR,b 波以及 PhNR/b 波的幅值显著较低($P<0.001$)。眼压升高降低了 PERG 与 PhNR 的振幅。
关键词:青光眼;电生理;明视负向反应

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Abstract

• The role of photopic negative response (PhNR) and pattern electroretinogram (PERG) was assessed as diagnostic indicator of glaucoma. Ten control subjects and 15 patients with early glaucoma underwent complete ophthalmological examination including visual acuity measurement, intraocular pressure (IOP) measurement, fundus examination and visual field examination. Pattern ERG and photopic full-field ERG were performed. Mean deviation (MD) and pattern standard deviation (PSD) means were significantly reduced in glaucoma group ($P<0.001$ and $P<0.01$). The amplitudes of PERG N95, PhNR, b-wave and the PhNR/b-wave ratio were significantly reduced ($P<0.001$). The rise in IOP resulted in reduction of PERG and PhNR amplitude.
• KEYWORDS: glaucoma; electrophysiology; photopic negative response
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INTRODUCTION

Glaucomais a group of diseases characterized by optic nerve damage and visual field loss. It causes progressive loss of vision due to retinal ganglion cells atrophy, either by necrosis or apoptosis[1]. The Early Manifest Glaucoma Trial 2 and the Ocular Hypertension Treatment (OHT) Study suggested that the progression of glaucoma is slowed down by reducing IOP and the elevated IOP is a major risk factor for developing glaucoma. About 25% to 30%, of the ganglion cells is already lost when visual field losses are apparent[2-3]. Early glaucoma diagnosis can detect patients with early retinal damage before visual field changes occur. Thus, therapy can be applied before irreversible retinal damage and visual field loss.

The pattern electroretinogram (PERG) reflects ganglion cell activity and is therefore a direct and promising approach to assist early detection of glaucoma. PERG assesses the function of retinal ganglion cells (RGCs) by isolating the magnocellular ganglion cell response using a reversing checkerboard or grating pattern with no change in average luminance over time. PERG was used successively in early diagnosis in primary open angle glaucoma (POAG) and ocular hypertension[4]. PERG amplitude reduction can appear before any significant visual field changes[5]. PERG was not used widely because it requires refractive correction, clear ocular media, good patient co-operation for proper placement of electrodes otherwise erroneous results can be produced.

In conventional flash ERG, the photopic negative response (PhNR) is the slow negative potential following the b-wave, originating from the inner retina[6]. The PhNR amplitude is associated with cone-related RGCs function and it may be compared with the N95 of the PERG. Full-field PhNR amplitude correlated with the mean deviation of the visual field[7]. Therefore, its use as a relative measure of the retinal ganglion cells function in glaucoma diagnosis in patients with

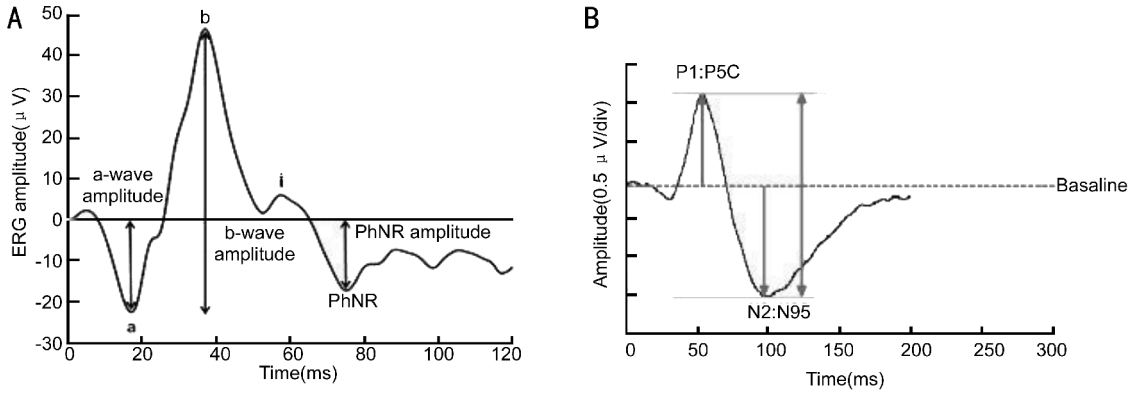

Figure 1 Diagram illustrating A: a full-field ERG trace, showing a-wave(a), b wave(b), i-wave (i), and photopic negative response (PhNR) amplitudes[9]; B: PERG tracing[5].

mild glaucoma. This study aimed to determine whether the PhNR elicited by transient white flash on white background and PERG were characterizing for glaucoma diagnosis in patients with mild glaucoma.

SUBJECTS AND METHODS

Patients were recruited from the outpatient clinic of the Research Institute of Ophthalmology and informed consent was obtained. Ten control subjects (five men and five women) and 15 patients (6 males and 9 females) with early glaucoma (MD ≤ -6.00 dB) underwent complete ophthalmological examination, best corrected visual acuity, anterior segment examination by slit lamp, IOP measurement by applanation tonometry. Fundus examination was done after full mydriasis to detect optic disc cupping and rim changes characteristic of glaucoma. Visual field was performed using Humphrey automated VF analyzer, with the central 24-2 strategy.

Inclusion criteria were subjects of early primary open angle glaucoma with high IOP (measured with Goldmann applanation tonometry at two different times) exceeding 22 mm Hg with additional risk factors such as glaucoma of the fellow eye or positive family history of glaucoma, normal and reliable visual field test results, as defined below, and early glaucomatous optic cupping. Exclusion criteria were best corrected visual acuity less than 6/9 (0.8 decimal), any secondary glaucoma (*e. g.* pigment dispersion or pseudoexfoliation syndrome), diabetic retinopathy or other disease capable of causing visual field loss or optic disc damage. Visual field examination (Humphrey field analyzer), and electrophysiological tests were done as follows.

Visual Field Criteria Visual field defects, measured by static automated perimetry (SAP, Humphrey Visual Field Analyzer, Humphrey Instruments, San Leonardo, CA). The SITA standard strategy was applied to program 24-2 white on white. Mean deviation (MD) was analyzed. The visual field defect was described as glaucomatous based on European Glaucoma Society guidelines[8] and classified as early with MD equal or less than -6.00 dB.

Electophysiological Examination Photopic ERG and Pattern ERG recordings were recorded binocularly using Retiscom system (Roland-Consult). The active (HK) electrode was placed in the lower fornix and a silver electrode placed close to the outer can thus for an ipsilateral temporal reference. A silver electrode at the midfrontal position, served as the ground. PERGs were recorded with black and white checkerboard pattern stimulus, reversing 4.286 times per second (square wave reversal, cycle time was 0.232 second) at a 97% contrast. The stimuli were generated on a monitor subtending viewing angle of 8.5 degree at a distance of 80 cm. The stimuli covered the whole screen, which was 30 cm wide and 37.5 cm high. The amplifier bandpass filters were 5-50 Hz.

Each patient was refracted and viewed the checkerboard with an appropriately adjusted refractive correction. The pupil was then dilated with phenylephrine hydrochloride 2.5% eye drops (Misr, Egypt) and tropicamide 1% eye drops (Alcon, Egypt). The single flash photopic ERG was recorded with a Ganzfeld stimulator. The white Standard Flash was used, with a flash intensity of 3 cd. m^{-2} at frequency of 0.3 Hz and cycle time of 3.3 second, the rods being suppressed by a white background with a luminance of 25 cd. m^{-2}.

The PhNR signal is the slow negative potential following a- and b- waves in photopic ERG. Amplitudes of waves were measured from baseline to the lowest point of the negative peak for PhNR and the a-wave and from the latter to the positive peak for the b-wave. The a-, b-wave and PhNR peak latencies were calculated from the flash onset to the peaks of waves. All electrophysiology traces were characterized by two negative and one positive deflection. The PERG P50-N95 was measured from P50 peak to N95 tough. The photopic ERG a-wave was measured from the baseline, the b-wave measured from a-wave trough to b-wave peak. The PhNR from baseline to the trough of the following negative wave. The PhNR ratio was calculated PhNR/b wave. Figure 1 (A and B) shows illustration of the ERG and PERG tracings.

RESULTS

All open-angle glaucoma patients were receiving ocular hypotensive therapy. Compared with the control group, the IOP was not significantly higher in the open-angle glaucoma due to effective medical treatment ($P=0.12$, t-test). MD

Table 1 Results of the examined groups

Group	Control(n=10 cases, 20 eyes)	Glaucoma(n=15 cases, 30 eyes)	P
Age(a)	45.3±7.54	48.13±7.46	0.197
IOP (mm Hg)	15.5±1.67	19.7±2.78	0.12
Cup/disc ratio	0.29±0.08	0.34±0.07	0.06
MD (dB)	−0.45±0.24	−2.7±0.98	<0.001[a]
PSD (dB)	1.5±0.11	3.50±1.29	<0.01[a]
a-wave (μV)	9.13±0.38	7.92±0.29	0.059
b-wave(μV)	44.75±3.42	40.13±4.01	<0.001[a]
PERG N95 (μV)	6.94±1.73	3.91±1.46	<0.001[a]
PhNR(μV)	18.23±2.07	11.79±3.49	<0.001[a]
PhNR/b wave ratio	0.408±0.04	0.294±0.07	<0.001[a]

Data expressed as mean±SD. MD: Mean deviation; PSD: Pattern standard deviation; PERG: Pattern electroretinogram; PhNR: Photopic negative response; dB: Decibel; μV: Microvolt; [a]P<0.05, t-test.

Table 2 Results of Pearson's test of linear correlation for examined tests

Electrophysiological parameters	MD		PSD		PERG N95		PhNR	
	r	P	r	P	r	P	r	P
PERG N95	−0.21	0.27	0.08	0.67	–	–	0.48	0.007[a]
PhNR	−0.16	0.41	0.067	0.72	0.48	0.007[a]	–	–
PhNR/b wave ratio	−0.20	0.30	0.053	0.78	0.39	0.03[a]	0.95	<0.001[a]

MD: Mean deviation; PSD: Pattern standard deviation; PERG: Pattern electroretinogram; PhNR: Photopic negative response; [a]P<0.05, Pearson's test of linear correlation.

and PSD means were significantly reduced in glaucoma patients as compared to control group (P<0.001 and P<0.01, t-test, respectively. There were no significant differences in the implicit times of the various ERG components for studied subjects, and therefore they have not been included. Glaucoma group showed significant reduced amplitudes of PERG N95, PhNR, b-wave and the PhNR/b-wave ratio, (P<0.001, t-test) (Table 1).

As for the correlation of MD and PSD with electrophysiological results, there was no significant correlation. Meanwhile, there was significant positive correlation between PERG N95, PhNR, PhNR/b-wave ratio (Table 2).

Figure 2 shows selected PhNR and PERG recordings of two cases with early glaucoma and a control subject.

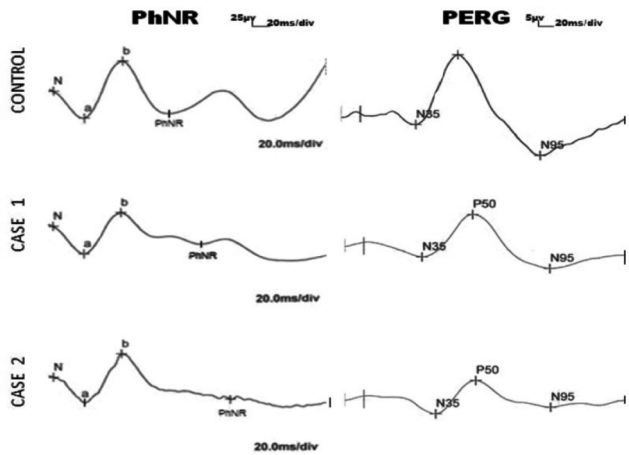

Figure 2 Selected PhNR and PERG recordings of two cases with early glaucoma and a control subject PhNR and N95 of PERG were reduced in the glaucoma cases as compared to normal recording.

DISCUSSION

In present study, the reduced electrophysiological parameters signified the early deficit in the ganglion cell function in spite of the minimal visual field loss. This was in agreement with previous studies[10]. It was found that PhNR amplitude and PhNR/b-wave amplitude ratio were significantly correlated with the ganglion cell complex thickness[10]. Previously, the full-field white flash PhNR amplitude was significantly reduced in experimental glaucoma and was significantly correlated to ganglion cell layer cells[11]. Compared to the PERG, the full-field PhNR is easier to record as it does not require refractive correction and a long foveal fixation[12].

In agreement to previousstudies[5,13], the highly significant correlation of the PERG P50-N95 with the PhNR suggested a common origin for these potentials.

The b-wave of the photopic PERG originates from cone bipolar cells and perhaps Muller cells. Although, it was reported to be less sensitive than the PhNR in distinguishing healthy from glaucomatous eyes[9-10], other studies [5,14] found b-wave deficit, which agreed to our study.

Similar to our study, Banitt *et al*[15] reported progressive PERG changes in glaucoma suspects were not correlated with significant visual field changes. Although a correlation between glaucomatous visual field defects and reduced PERG amplitude in the corresponding hemifield has already been reported[16], it is important to remember that standard PERG

is not appropriate for the detection of focal glaucomatous damage.

In conclusion, PhNR and PERG measurement may be promising in early glaucoma diagnosis. However, it should be confirmed on a larger group of patients with longer follow-up period.

REFERENCES

1 Sharma P, Sample PA, Zangwill LM, Schuman JS. Diagnostic tools for glaucoma detection and management. *Surv Ophthalmol* 2008; 53 (Suppl1):S17-S32

2 Tsaousis KT, Plainis S, Parry NR, Pallikaris IG, Tsilimbaris MK, Detorakis ET. Visual electrodiagnosis in glaucoma screening: a clinical study. *J Glaucoma* 2013;22(5):427-431

3 Georgiou AL, Guo L, Francesca Cordeiro M, Salt TE. Electroretinogram and visual-evoked potential assessment of retinal and central visual function in a rat ocular hypertension model of glaucoma. *Curr Eye Res* 2014;39(5):472-486

4 Karaskiewicz J, Drobek-Słowik M, Lubinski W. Pattern electroretinogram (PERG) in the early diagnosis of normal-tension preperimetric glaucoma: a case report. *Doc Ophthalmol* 2014;128(1):53-58

5 North RV, Jones AL, Drasdo N, Wild JM, Morgan JE. Electrophysiological evidence of early functional damage in glaucoma and ocular hypertension. *Invest Ophthalmol Vis Sci* 2010;51(2):1216-1222

6 Preiser D, Lagrèze WA, Bach M, Poloschek CM. Photopic negative response versus pattern electroretinogram in early glaucoma. *Invest Ophthalmol Vis Sci* 2013;54(2):1182-1191

7 Machida S, Toba Y, Ohtaki A, Gotoh Y, Kaneko M, Kurosaka D. Photopic negative response of focal electoretinograms in glaucomatous eyes. *Invest Ophthalmol Vis Sci* 2008;49(12):5636-5644

8 Kulkarni KM, Mayer JR, Lorenzana LL, Myers JS, Spaeth GL. Visual field staging systems in glaucoma and the activities of daily living. *Am J Ophthalmol* 2012;154(3):445-451.e3

9 Niyadurupola N, Luu CD, Nguyen DQ, Geddes K, Tan GX, Wong CC, Tran T, Coote MA, Crowston JG. Intraocular pressure lowering is associated with an increase in the photopic negative response (PhNR) amplitude in glaucoma and ocular hypertensive eyes. *Invest Ophthalmol Vis Sci* 2013;54(3):1913-1919

10 Machida S, Kaneko M, Kurosaka D. Regional variations in correlation between photopic negative response of focal electoretinograms and ganglion cell complex in glaucoma. *Curr Eye Res* 2015;40(4):439-449

11 ElGohary AA, Elshazly LH. Photopic negative response in diagnosis of glaucoma: an experimental study in glaucomatous rabbit model. *Int J Ophthalmol* 2015;8(3):459-464

12 Kremers J, Jertila M, Link B, Pangeni G, Horn FK. Spectral characteristics of the PhNR in the full-field flash electroretinogram of normals and glaucoma patients. *Doc Ophthalmol* 2012;124(2):79-90

13 Luo X, Frishman LJ. Retinal pathway origins of the pattern electroretinogram (PERG). *Invest Ophthalmol Vis Sci* 2011;52(12):8571-8584

14 Wilsey LJ, Fortune B. Electroretinography in glaucoma diagnosis. *Curr Opin Ophthalmol* 2016;27(2):118-124

15 Banitt MR, Ventura LM, Feuer WJ, Savatovsky E, Luna G, Shif O, Bosse B, Porciatti V. Progressive loss of retinal ganglion cell function precedes structural loss by several years in glaucoma suspects. *Invest Ophthalmol Vis Sci* 2013;54(3):2346-2352

16 Ventura LM, Golubev I, Feuer WJ, Porciatti V. Pattern electroretinogram progression in glaucoma suspects. *J Glaucoma* 2013;22(3):219-225