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CLINICAL INVESTIGATION

Efficacy of N95 amplitude of pattern electroretinogram measured from baseline to N95 trough in the traumatic optic neuropathy

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Abstract

Purpose To investigate the utility of selected pattern electroretinogram (PERG) parameters—including N95 amplitude and N95/P50 ratio, and a BL-N95 amplitude—in the analysis of visual function(s) and for predicting changes in retinal ganglion cell structures in traumatic optic neuropathy.

Study design A retrospective, observational case series performed at a single center.

Methods Forty-four eyes from 36 patients diagnosed with optic neuropathy were included. A BL-N95 amplitude was defined as the amplitude measured from baseline to the trough of N95. PERG and pattern visual evoked potential (pVEP) measures were acquired within 1 week after onset of optic neuropathies. To compare functional and anatomical changes, mean temporal peripapillary retinal nerve fiber layer (pRNFL) and average and minimum ganglion cell-inner plexiform layer (GC-IPL) thicknesses were measured using optical coherence tomography.

Results Thirty-six patients (20 men, 16 women; mean age 37.5 ± 17.6 years) were evaluated. The BL-N95 amplitude was significantly smaller than the N95 amplitude (1.01 ± 0.56 μV and 2.45 ± 1.02 μV, respectively; $p < 0.0001$). Both the N95 ($r = -0.38$, $p = 0.010$) and BL-N95 $r = -0.32$, $p = 0.029$) amplitudes were significantly correlated with visual acuity. Although P100 latency was not correlated with all PERG parameters, the N95 ($r = 0.32$, $p = 0.032$) and BL-N95 ($r = 0.41$, $p = 0.005$) amplitudes demonstrated a positive correlation with P100 amplitude in pVEP. PERG parameters, including the N95 and BL-N95 amplitudes, and N95/P50 ratio, were not correlated with pRNFL thickness in optical coherence tomography. Only the BL-N95 amplitude demonstrated a significant correlation with GC-IPL.

Conclusion The BL-N95 amplitude——measured from baseline to the trough of N95——was valuable in the analysis of visual function(s) and for predicting changes in retinal ganglion cell structures in traumatic optic neuropathy.

Keywords Optic neuropathy · Electrophysiology · Pattern electroretinogram · Pattern visual evoked potential

Introduction

There are several methods of analyzing functional changes in optic neuropathies including visual acuity, visual field measurements and electrophysiological tests. Among the electrophysiological tests, pattern electroretinogram (PERG) and photopic negative responses are used to assess ganglion cell activity.

Among the PERG parameters, N50 reflects macular function (on pathway) and N95 arises in the retinal ganglion cells (off pathway) [1, 2]. Conventionally, the amplitude of N95 is measured from the P50 peak to the trough of N95 [3]. However, because P50 may be affected in some patients with optic neuropathy, the N95 amplitude may not always prove an accurate way to evaluate retinal ganglion cells [4]. We investigated the efficacy of BL-N95 amplitude (from baseline to N95 trough) and analyzed the effectiveness of PERG in the analysis of visual function(s) and in predicting changes in retinal ganglion cell structures in optic neuropathies. In particular, we focused on parameters, including N95 amplitude and the N95/P50 ratio, and the BL-N95 amplitude, in patients with traumatic optic neuropathy (TON).

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Methods

This retrospective, observational case series was performed at a single center, approved by the Institutional Review Board of Kim's Eye Hospital (Seoul, Korea) and conducted in accordance with the tenets of the Declaration of Helsinki. Given the retrospective nature of the study and the use of anonymized patient data, requirements for informed consent were waived.

Forty-four eyes from 36 patients diagnosed with TON between January 2016 and May 2017 were included. All patients exhibited visual field defects and retinal nerve fiber layer defects in the affected eye verified by optical coherence tomography (OCT). In cases of unilateral optic neuropathy, relative afferent pupillary defect-positive patients were enrolled. Individuals with macular disorders, or a history of ophthalmic or glaucoma surgery, were excluded.

Basic ophthalmological examinations were performed. Visual acuity was calculated by LogMAR scale and off-chart visual acuity was defined as follows; finger count = 2.0, hand motion = 3.0, Electrophysiological tests, including pattern visual evoked potentials (pVEP) and PERG (RETIscan® system, Roland Consult), were performed simultaneously.

The stimulus, based on international society for clinical electrophysiology of vision standards, was a black and white reversing checkerboard with 48 min arc at a viewing distance of 1 m using cathode-ray tube (CRT) monitor. The mean screen luminance was 100 cd/m^2 with a contrast of 99% and full field display. The temporal frequency was 2.0 Hz and the mean luminance of the test room was 80 cd/m^2. The amplifier band-pass filters were set at 1–50 Hz. PERG was obtained by loop electrodes hooked into the lower fornix [3, 5]. Among the PERG parameters, N95 amplitude and N95/P50 ratio were analyzed. In addition, a BL-N95 amplitude was defined as the amplitude measured from baseline to the trough N95 (Fig. 1). P100 amplitude and latency were analyzed in pVEP. PERG and pVEP measures were acquired within 1 week after onset.

To compare functional and anatomical changes, OCT (Cirrus HD-OCT, Carl Zeiss Meditec) was performed to assess peripapillary retinal nerve fiber layer (pRNFL) and ganglion cell- inner plexiform layer (GC-IPL) thickness. Among several OCT parameters, mean and temporal pRNFL thickness, and average and minimum GC-IPL thickness were measured for 6 months or more following onset in order to record changes of permanent damage in retinal ganglion cells.

damage in retinal ganglion cells.

Data were analyzed using SPSS version 18.0 (IBM Corporation). Correlations between tests were analyzed using Spearman's correlation coefficient. Differences were considered to be statistically significant at $p < 0.05$.

Results

Thirty-six patients (20 men, 16 women; mean [± SD] age 37.5 ± 17.6 years) were evaluated. The BL-N95 amplitude was significantly smaller than the N95 amplitude (1.01 ± 0.56 µV and 2.45 ± 1.02 µV, respectively; $p < 0.0001$) (Fig. 2).

The results of PERG were compared with functional tests including visual acuity and pVEP. Both the N95 amplitude ($r = -0.40$, $p = 0.001$) and the BL-N95 amplitude ($r = -0.38$, $p = 0.012$) revealed a significant correlation with visual acuity (Fig. 3). Although P100 latency and P100 amplitude were not correlated with the two parameters (N95 amplitude and N95/P50 ratio), BL-N95 amplitudes demonstrated a positive correlation with P100 amplitude ($r = 0.30$,

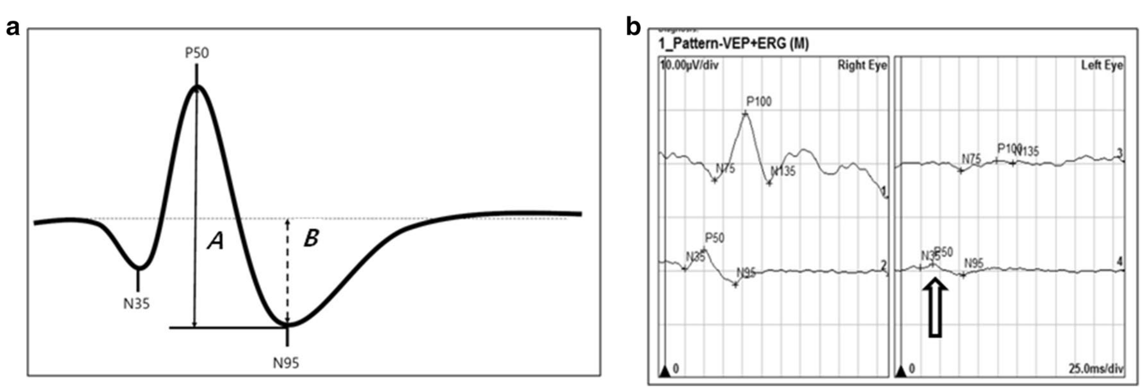

Fig. 1 **a** measurement of the BL-N95 amplitude. *A:* N95 amplitude (from peak of P50 to trough of N95). *B:* the BL-N95 amplitude (from baseline to trough of N95). **b** The results of pattern visual evoked potential and pattern electroretinogram in a patient with traumatic optic neuropathy. Not only N95 but also P50 reduced in the left eye (open arrow)

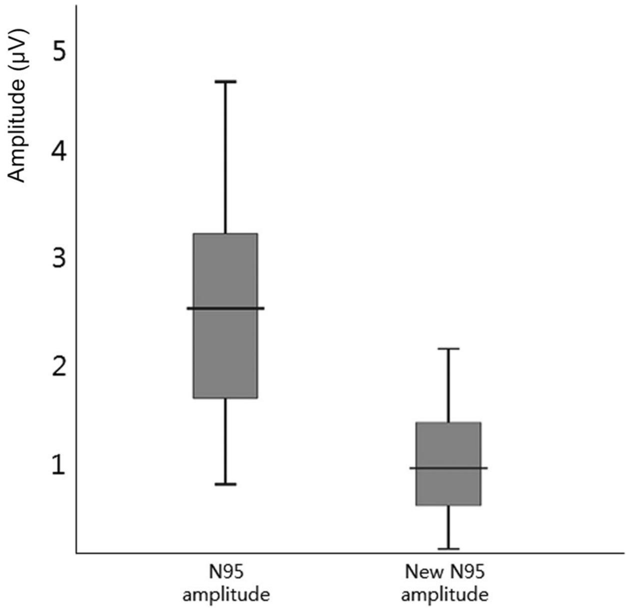

Fig. 2 Comparison of amplitude between N95 and the BL-N95 (2.45 ± 1.02 µV vs. 1.01 ± 0.56 µV; $p < 0.0001$)

$p = 0.045$) and a significant negative correlation with P100 latency in pVEP ($r = 0.38$, $p = 0.010$) (Table 1).

As predictors of anatomical change(s), PERG parameters, including N95 amplitude, BL-N95 amplitude and N95/P50 ratio, were not correlated with pRNFL thickness in OCT. Only the BL-N95 amplitude demonstrated a significant correlation with GC-IPL thickness (Table 2).

Discussion

The present study revealed that the BL-N95 amplitude, measured from baseline to trough of N95, can be valuable in the analysis of visual functions and predicting changes in retinal ganglion cell structures in traumatic optic neuropathy.

Among the PERG parameters, the N95 and BL-N95 amplitudes demonstrated a correlation with visual acuity; however, the N95/P50 ratio was not correlated with visual acuity. These results are similar to previous reports. Atilla et al. [6] also report no significant differences in N95/P50 ratio regardless of whether the eyes were affected by optic neuropathy. This may be explained by the concomitant reduction in P50 and N95 amplitude in eyes with optic neuropathies [7, 8].

Several studies report that the delay in latency and reduction of amplitude in VEP may be related to the N95 component of PERG [6, 9, 10]. Interestingly, in the present study, P100 latency and P100 amplitude had a significant correlation with BL-N95 amplitudes. Patients enrolled in the present study experienced traumatic optic neuropathy, for which the vulnerability to injury in retinal ganglion cells is greater than in other optic neuropathies [11].

The prediction of structural changes is important in optic neuropathies. OCT isregarded as a useful method of analyzing retinal ganglion cells. However, structural changes, including optic disc pallor and RNFL loss, observed in OCT appear to be normal at onset. Reduction in pRNFL and ganglion cell complex thickness begins to diminish 2 weeks after trauma and exhibits no change at 20 weeks [12]. Although electrophysiological tests, such as VEP and PERG, are somewhat difficult to analyze, the abnormal findings in these tests are present in the early stages, and could be helpful in interpreting the status of optic neuropathies [11]. Yukita et al. [13]. report that, using OCT in rodent

Table 1 Correlation between pattern electroretinogram (ERG) and P100 latency and amplitude in pattern visual evoked potential

	Pattern ERG		
	N95 amplitude	N95/P50 ratio	BL-N95 amplitude
P100 latency	− 0.16 (0.275)	− 0.07 (0.640)	− 0.38 (0.010)
P100 amplitude	0.20 (0.185)	0.13 (0.387)	0.30 (0.045)

Data presented as correlation (i.e., *r*) (*p* value)

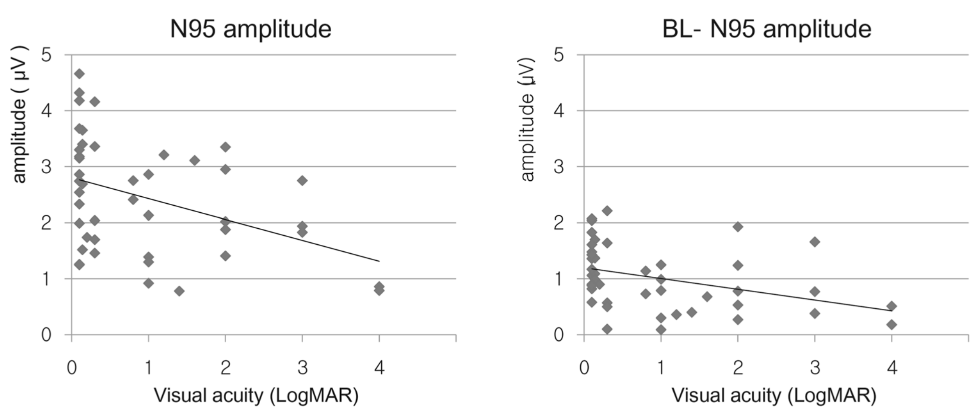

Fig. 3 Correlation between visual acuity and parameters of pattern electroretinogram. N95 amplitude and BL-N95 amplitude demonstrate significant correlation with visual acuity ($r = -0.40$, $P = 0.001$ and $r = -0.38$, $p = 0.012$, respectively). (LogMAR visual acuity; finger count = 2.0, hand motion = 3.0 and light perception = 4.0)

Table 2 Correlation between pattern electroretinogram (ERG) and optical coherence tomography results

Parameter	Pattern ERG		
	N95 amplitude	N95/P50 ratio	BL-N95 amplitude
Mean pRNFL thickness	0.21 (0.263)	−0.07 (0.688)	−0.05 (0.791)
Temporal pRNFL thickness	0.26 (0.174)	−0.10 (0.602)	0.35 (0.060)
Average GC-IPL thickness	0.12 (0.526)	−0.10 (0.591)	0.43 (0.021)
Minimum GC-IPL thickness	0.19 (0.333)	−0.08 (0.667)	0.50 (0.007)

Data presented as correlation (i.e., r) (p value). pRNFL: peripapillary retinal nerve fiber layer; GC-IPL: ganglion cell-inner plexiform layer

optic nerve crushing model, changes in electrophysiological test using positive scotopic response appeared earlier (day 3) than changes in inner retinal thickness (day 10). In glaucoma models, PERG can be altered before changes of retinal ganglion cells [14]. Therefore, PERG in the TON could be a method to detect early changes, while PERG is also correlated with structural changes in the optic nerve [15]. Optic neuropathies originate from damage to retinal ganglion cells, and these defects can be evaluated using pRNFL and GC-IPL complex thickness observed on OCT.

The present study analyzed PERG in the early stage (within 1 week after onset) and compared it with OCT findings in the chronic state (≥ 6 months) to predict prognosis of anatomical changes. This study revealed a significant correlation between GC and IPL complex thickness and PERG, especially among PERG parameters; however, the BL- N95 amplitude appeared to be only a prognostic factor of anatomical change(s) after optic damage. GC-IPL thickness is measured in the macula and is related to central visual acuity. Thus, PERG obtained from the central macula is more sensitive to changes in GC-IPL thickness. Bowd et al. [16]. report that steady state PERG is weakly associated with macular ganglion cell complex and RNFL thicknesses; however, the weak correlation between PERG and these thicknesses may be due to the summation of PERG. Therefore, to increase the utility of PERG, more selective parameters may be needed. P50 reflects macular function and can be a confounding factor in measuring N95 amplitude [17]. Thus, the effect of P50 is excluded from the measurement of the BL-N95 amplitude and is more valuable in assessing retinal ganglion cells.

This study has limitations. First, PERG was obtained within 1 week, however, PERG amplitudes can be normal in the early stage [18]. Secondly, poor fixation due to decreased visual acuity could decrease the amplitude of PERG. Nevertheless, this study aimed to investigate the efficacy of BL-N95 amplitude compared to N95 amplitude in the TON and these limitations could not significantly affect the results of the study.

In conclusion, the BL-N95 amplitude not only reflect visual function(s) but can also predict anatomical changes after the onset of traumatic optic neuropathy.

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Conflicts of interest K. H. Kim, None; U. S. Kim, None.

Informed consent For this type of study informed consent was not required.

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