

# Demonstration of reversible retinal ganglion cell dysfunction in inflammatory optic neuropathies utilizing pattern electroretinography

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Received: 2016-05-12

Accepted: 2016-08-18

**DOI:10.18240/ijo.2017.02.24**

Bach A, Kay MD. Demonstration of reversible retinal ganglion cell dysfunction in inflammatory optic neuropathies utilizing pattern electroretinography. *Int J Ophthalmol* 2017;10(2):321-324

## Dear Editor,

I am Dr. Austin Bach from Larkin Community Hospital in South Miami, Florida, USA. I am writing to you to present three cases of inflammatory optic neuritis that was followed to resolution using pattern electroretinography (PERG).

The use of standard PERG for assessment of ganglion cell dysfunction in various optic nerve disorders is well established<sup>[1-2]</sup>. However, a relatively new modification of this technology has been designed which permits the performance of a PERG through electrodes and allows for rapid data acquisition and user friendly interpretation of the results<sup>[3-4]</sup>. The PERG optimized for glaucoma screening (PERGLA), "Glaid" (Lace Elettronica, Pisa, Italy), which was the version of the machine that was used in these cases, uses skin electrodes vs the corneal electrodes leading to more patient comfort, but a reduction in amplitude and signal to noise ratio. This new emerging office-based technology was introduced as a means of potentially providing early detection of ganglion cell dysfunction in patients with pre-perimetric glaucoma<sup>[5]</sup>. This technique has been found to be a reproducible and useful complementary clinical tool for identifying the presence of glaucoma and for monitoring disease progression<sup>[6]</sup>.

Analyzing the data presented by the PERGLA has been previously described<sup>[3]</sup>. The waveform in the left chart was obtained through three sets of stimulation by the PERGLA with the average of 600 artifact-free time periods (elevated area of the sinusoidal curve) with user-defined pauses (depressed area of the sinusoidal curve) of both the right and left eyes. The polar diagram with box plots in the charts on the right side shows the

age predictive normative data (inside the box). Patients with a decrease in amplitude of response will have their response shown under the normative box.

Our first case is a 44-year-old woman presented with a one week history of decreased vision affecting her left eye associated with ipsilateral ocular discomfort. There was no prior history of demyelinating symptoms and past medical history was unremarkable.

On examination, corrected visual acuity was 20/20 OD and 20/50 OS. Color vision was 8 out of 8 OU using Ishihara plates. A left afferent pupillary defect was present. Humphrey visual field (HVF) was normal in the right eye while there was a moderate inferior arcuate scotoma with mild superior patchy depression OS (Figure 1B). The optic nerve was sharp and pink OU with a cup-to-disc ratio of 0.5 OD and 0.4 OS. No vitreous cells were present in either eye. The fundus was otherwise unremarkable OU. PERG was found to be normal in the right eye and demonstrated decreased amplitude on the left consistent with ganglion cell dysfunction which was confirmed as being sub-normal on the box plot (Figure 1A).

A clinical diagnosis of optic neuritis was made and a magnetic resonance imaging (MRI) was obtained which identified abnormal enhancement of the proximal third of the left optic nerve consistent with optic neuritis. As there were no definite demyelinating plaques in the brain, the patient was observed clinically without steroid treatment.

On follow-up examination one week after presentation, visual acuity had improved to 20/30 OS with moderate improvement of the HVF that now demonstrated significant resolution of the inferior field defect and mild residual patchy superior field loss (Figure 1D). PERG was repeated and had normalized in the left eye although the amplitude of the response remained slightly diminished in the left eye as compared to the right, though the amplitude had returned to be in the normative range based on the box plot (Figure 1C).

Our second case is a 73-year-old woman noted painless loss of vision affecting her left eye one day prior to presentation. Vision progressively worsened following onset. She denied symptoms of giant cell arteritis. Past medical history was significant for hypertension and hypercholesterolemia. On examination, corrected visual acuity was 20/25 OD and 20/100 OS. Color vision was 8 out of 8 OD and 0 out of 8 OS. A left

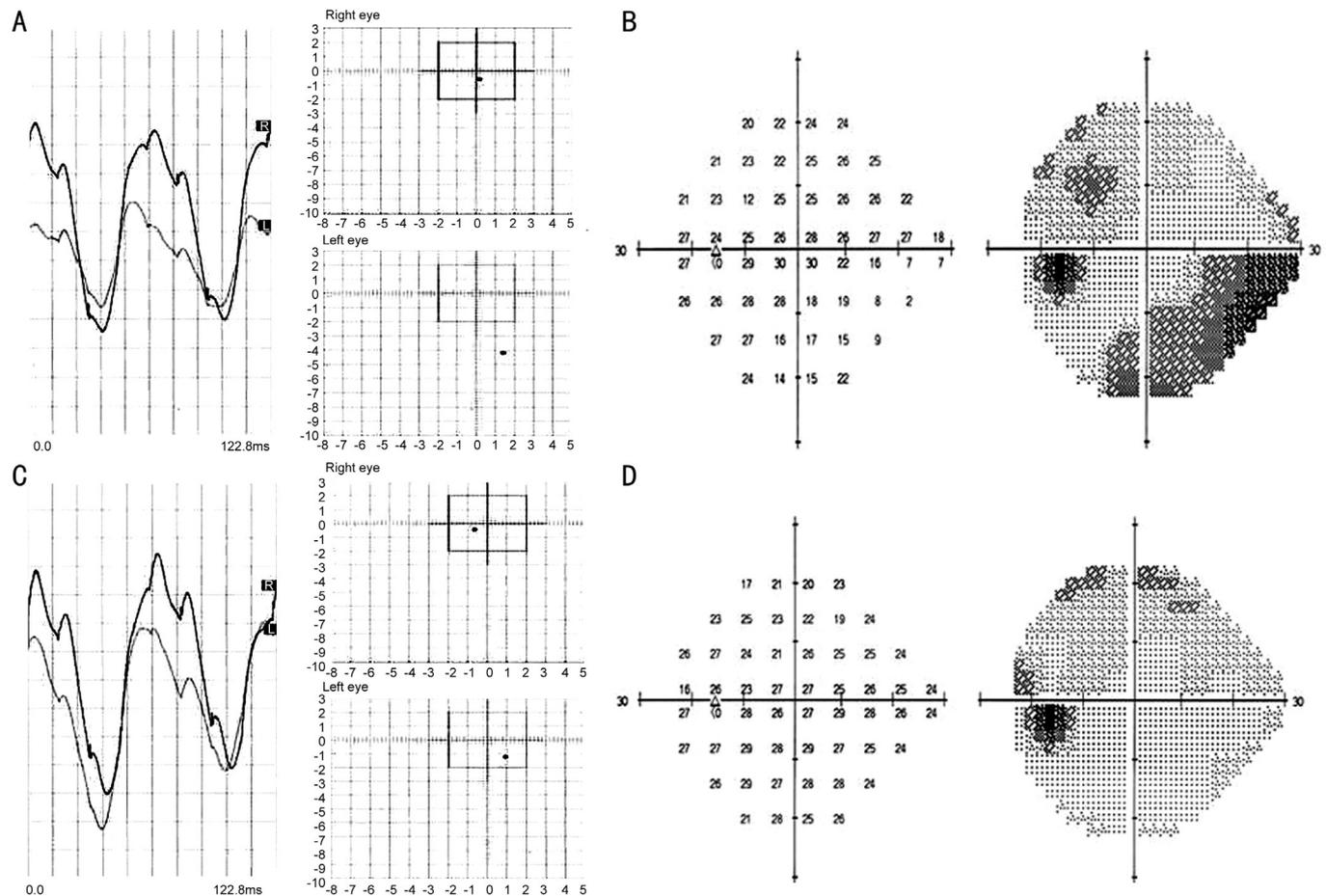


Figure 1 PERG (A) and HVF (B) on presentation, and PERG (C) and HVF (D) 7d later.

afferent pupillary defect was present. HVF was essentially normal in the right eye while there was severe generalized depression OS with the study in the left eye being unreliable secondary to multiple false negative errors. The optic nerve was sharp and pink OU with a cup-to-disc ratio of 0.5 OD and 0.1 OS. The fundus was otherwise unremarkable OU.

A diagnosis of a retrobulbar optic neuropathy was made, and an MRI of brain and orbits was obtained in addition to acute phase reactants. Prednisone was initiated at a dosage of 100 mg orally on a daily basis pending the results of this evaluation.

The MRI identified enhancement of a 10 mm segment of the intraorbital left optic nerve sheath consistent with orbital pseudotumor/perineuritis. MRI of brain revealed chronic ischemic white matter changes without evidence for acute pathology. Erythrocyte sedimentation rate was 15 mm/h, C-reactive protein 10.4 (upper range normal 4.9), and a platelet count of 373 000/cubic mm.

The patient returned 5d later noting that vision began to improve by the morning following her initial visit having taken her first dose of prednisone the prior evening with progressive visual improvement on a daily basis thereafter. On exam, visual acuity was 20/25 OU, color vision was 7.5 of 8 OU. A left afferent pupillary defect persisted. The optic nerve remained sharp and pink. HVF was unreliable in the left eye with multiple false positive errors and fixation losses and

moderate inferonasal depression and mild patchy depression elsewhere (Figure 2B). PERG was normal in the right eye and demonstrated significantly reduced amplitude in the left eye plotted to be sub-normal which was consistent with ganglion cell dysfunction (Figure 2A). Prednisone was tapered by 10 mg per week.

Two weeks later, the patient felt her vision had returned to normal. Visual acuity was 20/20 OS with 8 out of 8 color plates correctly identified. A left afferent pupillary defect remained. HVF was again unreliable with multiple fixation losses, false positive errors, and false negative errors and could not be interpreted (Figure 2D). PERG was repeated and although the results were in the normal range in each eye, the amplitude in the left eye remained depressed relative to the right (Figure 2C). Our final case is a 22-year-old white female presented with a 5-6d history of decreased vision OS associated with pain on eye movement. There was no prior history of demyelinating symptoms. MRI identified left optic nerve enhancement without demyelinating plaques in the brain.

On exam, corrected acuity was 20/30 OD and hand motion/barely counting fingers @6 inches OS. Color vision was 8/8 OD and 0/8 OS. A left afferent pupillary defect was present. HVF revealed mild non-specific superior depression OD and was extinguished OS (Figure 3B). The right optic nerve was sharp and pink with C:D of 0.4, while the left optic nerve was

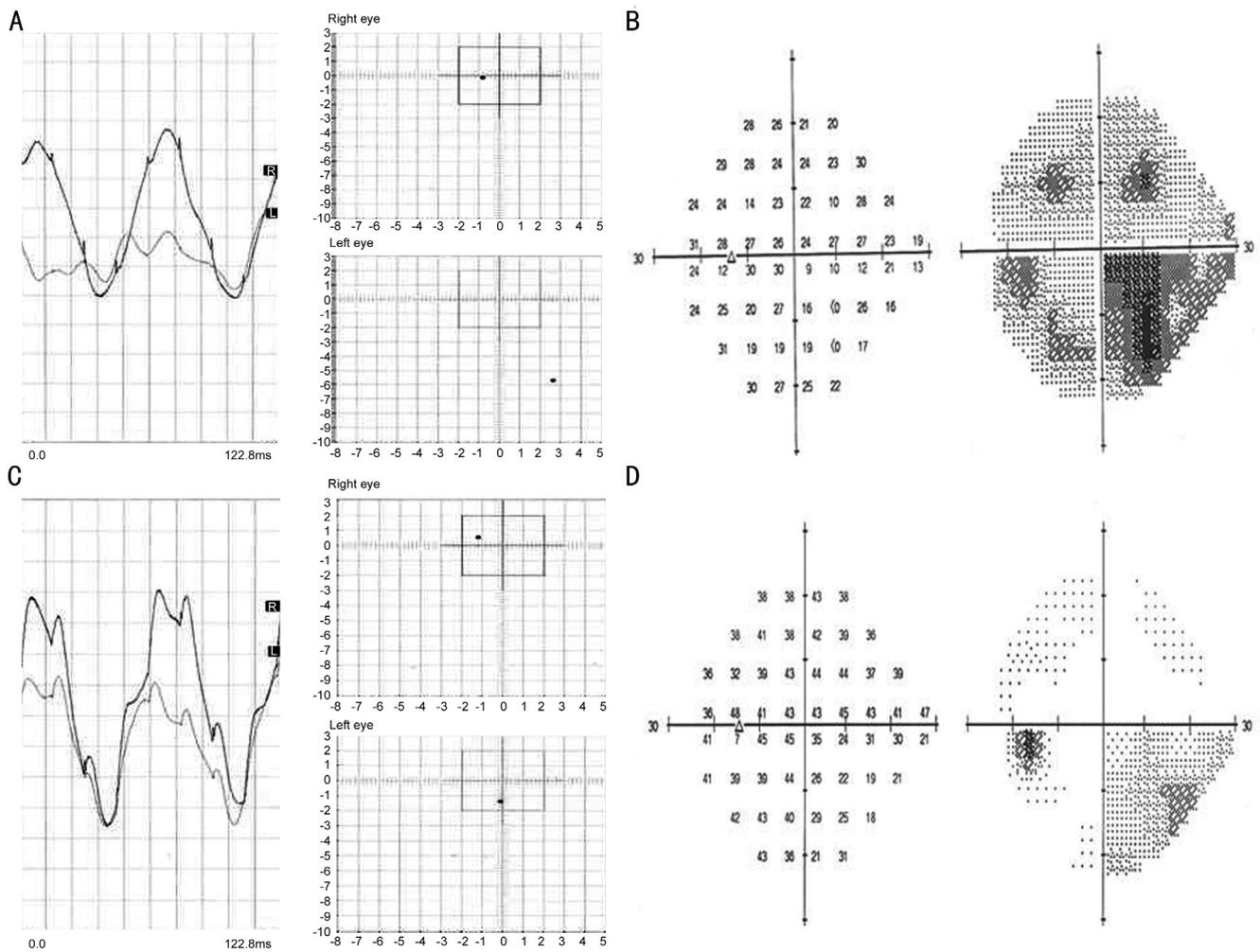


Figure 2 PERG (A) and HVF (B) on 5d of steroids, and PERG (C) and HVF (D) 14d after starting steroids.

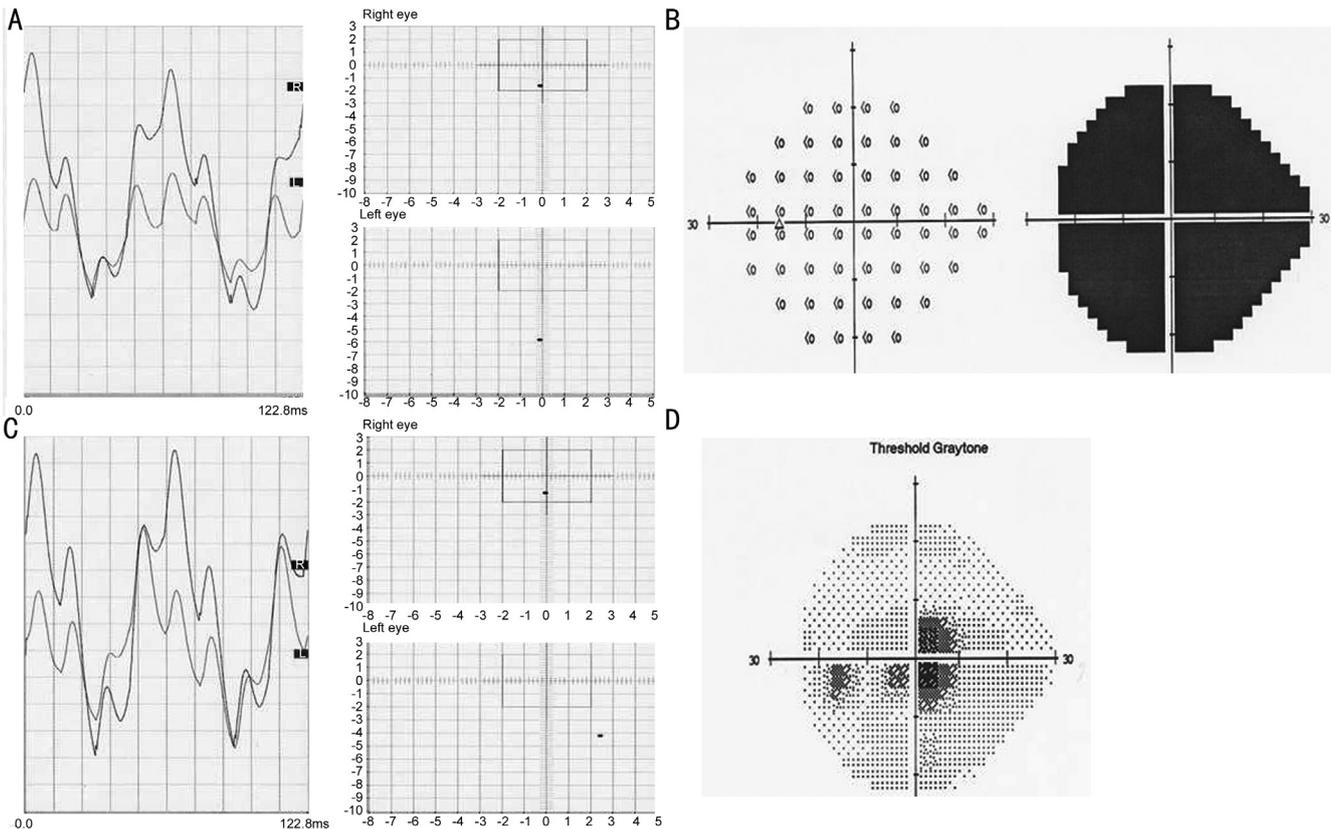


Figure 3 PERG (A) and HVF (B) on presentation, and PERG (C) and HVF (D) 14d after steroids.

pink with mild edema. PERG was normal OD and significant reduction in amplitude OS falling outside of the normative data (Figure 3A).

A 3d course of IV solumedrol followed by an 11d prednisone taper was administered with the patient noting subjective improvement on the evening of the first dose of intravenous steroids.

On follow-up, 2.5wk later, acuity was 20/30 OD and counting fingers @6 feet. OS with a central scotoma on HVF. Follow-up PERG demonstrated significant improvement in amplitude OS, but remained significantly depressed from the normative data (Figure 3D). The patient failed to return for subsequent follow up.

These cases represent the first report in which a relatively new office-based PERG technology has been demonstrated to be useful in monitoring recovery of visual function in the setting of inflammatory optic neuropathies. Two patients demonstrated normalization of their PERG paralleling their full recovery of optic nerve function as assessed *via* other standard measures such as visual acuity and HVF, while the third demonstrated improvement, albeit still reduced in amplitude, consistent with the incomplete recovery of optic nerve function, at most recent follow-up. Furthermore, in one of our patients (case 2), use of this technology provided an objective means of following recovery of ganglion cell function in an individual who could not be reliably monitored with serial HVFs secondary to poor field testing technique.

Whether this technology is applicable to the evaluation of non-glaucomatous optic neuropathies has not been well established, although a recent report did demonstrate recovery of ganglion cell function as assessed by PERG in three patients who underwent resection of a pituitary tumor abutting the optic chiasm<sup>[7]</sup>. PERG has also been shown to be a useful diagnostic tool in experimental models for optic neuritis<sup>[8]</sup> as well as having potential for other types of optic neuropathies<sup>[9]</sup>. We have now applied this technology to three patients with inflammatory optic neuropathies, and have performed serial PERG studies as their optic neuropathy resolved demonstrating progressive improvement on PERG studies.

Thus, the PERG technique may prove useful as an adjunctive objective measure for monitoring progression and/or resolution of glaucoma and other optic neuropathies in patients who are consistently unreliable when performing HVF. Further studies will be helpful in determining whether this new testing paradigm will be of benefit in monitoring for progression or recovery of ganglion cell function in other non-glaucomatous optic neuropathies including compressive lesions of the optic apparatus, ischemic optic neuropathy, papilledema, and toxic optic neuropathies.

### ACKNOWLEDGEMENTS

**Conflicts of Interest:** Bach A, None; Kay MD, None.

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