Electrophysiology in Vision

How VEP and ERG Testing Can Impact Your Treatment Decisions

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Electrophysiology in Eye Care

What do you think of when you think of electrophysiology?

How about when you think of EKG?

Electrophysiology of Vision

ERG
Electroretinogram

VEP
Visual Evoked Potential

Caveat for all Imaging devices

Electrical activity of the retina
Electrical activity of the visual cortex
Electrophysiology
Of
Vision

ERG
Electroretinogram

VEP
Visual Evoked Potential

Electrical activity of the retina

Electrical activity of the visual cortex

pERG
Pattern-Electroretinogram

fERG
Flash-Electroretinogram

NEURO-PHYSIOLOGY
Phototransduction
Conversion of light into electricity

NEURO-PHYSIOLOGY

Electrophysiology objectively measures strength and speed of the visual signal to the brain (VEP) or retina (PERG)
ISCEV

International Society for Clinical Electrophysiology of Vision

Clinical Applications in Eye Care
- Inherited retinal dystrophies
- Vascular diseases including diabetes
- Opaque media or trauma
- Retro bulbar neuritis
- Unexplained visual loss
- Infant with questionable vision
- Toxic and nutritional eye disease
- Glaucoma
- Suspected intracranial lesion

PREVIOUS LIMITATIONS
- Test time was approximately 45 minutes
- Required highly trained operators
- Limited to large research institutions
- Required highly trained neurophysiologists

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Time, Space, Cost Continuum
- Actual test time is considerably shorter
- Does not require highly trained operators
- Easy to use, intuitive software
- Comfortable for the patient, convenient for doctor and staff

VEP MADE SIMPLE

Visual Evoked Potential (VEP)
Visual - patient observes a visual stimulus
Evoked - generates electrical energy at the retina
Potential - measure the electrical activity in the visual cortex

Objective measurement of the function of entire vision system; No verbal response or “button pushing” like visual field tests

International VEP Standard
- Time (latency) is measured in milliseconds (ms)
- Amplitude is measured in microvolts (µV)
- N75-P100-N135 Complex
- N75: Negative pulse around 75ms
- P100: Positive pulse around 100ms
- N135: Negative pulse around 135ms
Clinical Applications

- Clarify Differential Diagnosis – Is it Systemic, Trauma or Ocular?
- When Standard Tests are Unattainable or Unreliable – Visual Field Can’t be Performed or Results are Unreliable
- Other Tests are Inconsistent or Borderline – Patient Symptom and/or Test Results are Equivocal
- Monitor Subclinical Ophthalmic Disease – Functional Changes

Why VEP?

- Many optic nerve diseases are asymptomatic because central vision is not affected until late in the disease
- Diagnosis and management of optic nerve disorders are often based on structural or subjective visual field tests

VEP is an objective, functional test that can help discriminate between healthy and glaucomatous eyes

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Iscev Standards

VEP –

“Visual evoked potentials (VEPs) can provide important diagnostic information regarding the functional integrity of the visual system.”

Where Does Glaucoma Begin?

Researchers at UCSD, Vanderbilt University, and the University of Toronto claim glaucoma begins in the LGN and is later seen as progression measured by visual field and structural changes measured by OCT, GDX, HRT, etc.
Led by Robert N. Weinreb, M.D., a team of scientists at UCSD’s Glaucoma Center recently reported that glaucoma is not a disease restricted only to the eye. Their study, “Loss of LGN Neurons in Glaucoma,” appeared in the March 2000 issue of Archives of Ophthalmology.

Though commonly misunderstood as a disease of “increased eye pressure,” the hallmark of glaucoma is the optic nerve fiber loss, regardless of the pressure.

Ninety percent of the optic nerve fibers from the eye terminate in the lateral geniculate nucleus. The visual cortex detects the electrical signals, processes them, and provides us with our sense of sight.

Dr. Weinreb’s group, including lead author Yeni Yucel, M.D., Ph.D. (a neuropathologist and UCSD Postdoctoral Glaucoma Fellow at the time, presently the Director of Ophthalmic Pathology at the University of Toronto), found in a primate model that there was extensive loss of nerve cells in the lateral geniculate nucleus with progressive glaucoma, a process known as transneuronal degeneration. According to Dr. Weinreb, “by studying changes in the brainstem we may better understand what causes vision loss in glaucoma. This information could be critical in helping researchers determine how to prevent vision loss in patients with known glaucoma or at risk for developing it.”

**VEP and Glaucoma: Well Defined Science**

**The Visual Evoked Potential in Glaucoma and Ocular Hypertension: Effects of Check Size, Field Size, and Stimulation Rate**


“Increased pattern VEP latency was significantly correlated with both the severity and location of visual field defects and the degree of cupping and pallor of the optic disc.”

“Glaucoma has also been reported to affect the VEP by causing both reductions in amplitude and increases in latency.”

“Under this stimulus condition, 16 of the 30 eyes with glaucomatous field defects had abnormally long VEP latencies. None of the VEPs from the normal subjects had abnormally long latencies. It is of particular interest that 9 out of 40 of the eyes of ocular hypertensive patients had abnormally long VEP latencies. These nine eyes were from five patients.”

“In spite of these significant correlations, it should be noted that nearly half of the eyes with glaucomatous field defects (14 of 30 eyes) generated normal VEPs even though many of these defects clearly encroached upon the macula. We performed additional tests on 9 of these patients in an attempt to understand why these patients generated normal VEPs.”
“Reducing the intensity of the stimulus display by as much as 1.5 log units—to the range of the targets used to map the visual fields—caused abnormal VEPs (either abnormally long in latency or unrecordable) in five of these nine patients.”

“The finding that is of clinical importance is the presence of abnormally long VEP latencies in some patients with ocular hypertension. The abnormal prolongation of VEP latency in these eyes may reflect subclinical optic nerve lesions that have not been uncovered with other techniques.”

**Additional Clinical Papers**


**Glaucomatous Brain Damage**

- **VEP (Function)**
  - **OCT HRT GDX**
  - **Eye**
  - **Brain LGN**
  - **Stress (OHT)**

**Detecting Damage Before Treatment**

- **OCT HRT GDX**
- **VEP**
- **dead**
- **Buffering**
- **Alive**

**After Treatment**

- **OCT HRT GDX**
- **VEP**
- **dead**
- **Alive**
- **Gliaoma**
Understanding VEP Wave:

Normal

Abnormal

Reading Results: Normal

Case Study 1 – unreliable visual field

Introduction
- 70 year old white female
- Glaucoma suspect for elevated IOP’s
- General health history unremarkable; mother has Open Angle Glaucoma

Findings
- Best Corrected Acuities 20/25 OD OS
- Pupils and ocular motilities normal
- Slit lamp exam unremarkable and angles were open to grade IV OU
- Intraocular pressures at 4:30 PM were OD 23mmHg and OS 21mmHg
- Low reliability on visual field
- Central corneal thicknesses 506 and 507

Case Study 1

- Humphrey 24-2 Visual Field Testing showed a slight depression in the inferior Bjerrum area, and borderline GHT findings although this field was somewhat unreliable
- OS visual field was without defect
- 2nd visual field equally unreliable

Case Study 1

- Optic nerve cupping was .50 OD and .35 OS
- HRT scans normal
Case Study 1: VEP Aids in Decision to Treat Early POAG

- VEP studies revealed increased latency at 15% contrast level OD.
- Normal 85% contrast level normal OD.
- Both 15% and 85% normal OS.

Diagnosis and Treatment

- The ability to obtain a new objective measurement of optic nerve function by performing a VEP is significant in the decision to treat patients at the earliest level of POAG.

- Tx: Lumigan 0.01% 1 gtt QHS OU
- Follow up visit one month.
- Repeat at 6 months with 10-2 VF.

Case Study 2 – borderline for treatment

Introduction
- 45 year old white male
- General health, eye health and family health histories unremarkable
- Routine eye exam without significant complaints.

Findings
- Best corrected visual acuities with a small compound myopic correction of 20/20 OD OS.
- Pupils, color vision, motilities, and muscle balance normal.
- Intraocular pressures at 3:30 pm were 15mmHg in each eye.
- Asymmetric cupping on Fundoscopic exam as determined with a 78 D lens of .65 OD and .40 OS.
- Intraocular pressures at 10:30 in the morning were 15mmHg OU.
- Central corneal thickness was 550 OD and 550 OS.
- Gonioscopic view of the angles was open to the ciliary body OU with a 30 degree approach angle and grade I pigmentation.

Case Study 2 (cont.)

- Threshold Humphrey 24-2 visual fields full without defects OD OS.
- HRT optic nerve scans confirmed asymmetric cupping and findings were abnormal OD and borderline OS.

Case Study 2 (cont.)

- VEP studies revealed both 15% and 85% normal OD.
- Both 15% and 85% normal OS.

Typically most clinicians would have considered treating a patient of this type.

Case Study 3

Introduction
- 56-year-old black female
- O.D. is -5.75 – 0.50 x 15 with 20/20 acuity.
- O.S. is -5.75 – 0.25 x 180 with 20/20 acuity.
- Mild cortical cataracts.
- No apparent retinal pathology.
- No significant medical or ocular history.
- Patient states her vision is decreasing and she “just can’t see right.”

Case Study 3

- VEP allows for an objective assessment in addition to anatomy that supports monitoring instead of Tx.
Case Study 3

Normal optic nerve appearance

Case Study 3

Cirrus OCT retinal nerve fiber layer scan
Abnormal sector plot analysis on right eye
Superior RNFL defect on right eye
No clinically significant asymmetry

Case Study 3

Visual Field Exam
Abnormal VEP waveforms in each eye
Delayed P100 peak times in both high-contrast and low-contrast VEP responses
N75-P100-N135 complex is abolished in the low-contrast response in the left eye
Clinically significant asymmetry

Case Study 3

Diagnosis and Treatment
Patient was referred out for an MRI
MRI results found a cavernous hemangioma

Medical Decision Making:
In patients with subjective visual disturbances VEP can be a valued adjunct to traditional imaging
Normal VEP test results may suggest a conservative approach such as monitoring (i.e., temporary cessation of the diagnostic program).
Abnormal VEP test results suggest a continuation of the diagnostic program with one or more of the following treatment options:
- Confirm all abnormal findings within 1-2 weeks
- Brain, optic nerve, orbital imaging, and/or angiography
- Referral as appropriate

Case Study 3

Misinterpretation artifacts
- Localized losses of RNFL or macular thickness classified as normal due to averaging of thickness values by quadrant, sector, or hemisphere
- Misinterpretation of shadow artifacts
Myopia = “Red Disease”

- There is a higher percentage of abnormal diagnostic classification since the RNFL normative databases typically do not include moderate and high myopes.
- Myopic eyes are also associated with many other artifacts such as difficulty in acquiring a good image due to excessively long axial length or myopic retinal schisis affecting peripapillary RNFL thickness.

**VEP – Summary for Use**

**VEP** is an objective, functional test that can help discriminate between healthy and diseased eyes.

- Differentiate ocular from systemic, trauma or other conditions for co-management.
- Diagnosis and management of ophthalmic concerns.
- Alternative to VF or VA (need reliable results for diagnosis and treatment).
  - Visual Field Limitations 368.40
  - Visual Disturbance 368.10
- Questionable vision or diagnostic inconsistencies.
  - Conversion disorder (malingering) 300.11
  - Visual Disturbances 368.xx
  - Optic Nerve and Pathway disorders 377.xx
- Subclinical vision disorders for diagnosis and management.
  - Disorders affecting optic nerve 377.xx
  - MS/Optic neuritis 340
  - Optic neuropathies 377.xx
  - Unexplained vision loss 358.11
  - Transient visual loss 368.12
  - Visual field defects 368.xx
  - Amblyopia/Strabismus 368.0x
  - Traumatic Brain Injury 850-853.xx

**How Does pERG Work?**

Pattern electroretinogram (pERG) is an electrical recording of retinal function in the macula and ganglion cells stimulated by contrast-reversing patterns, usually black and white.
**Pattern Electroretinogram (pERG)**

- pERGs are electrical signals that are a measure of the electrophysiological activity in the ganglion cells in the retina.
- Can help improve sensitivity and specificity in diagnosing neuropathies and maculopathies like macular degeneration and glaucoma when used in conjunction with other tests.
- Can also help the clinician differentiate between retinal and optic nerve disorders when used in conjunction with Visual Evoked Potential (VEP).

Clinically, pERGs can be used in patients with abnormal pattern VEPs to establish if a central retinal disorder is present and thus differentiate between retinal and optic nerve dysfunction as a cause for the VEP abnormality.

It can also be used to detect and monitor dysfunction of retinal ganglion cells caused by conditions such as glaucoma, optic neuropathies and primary ganglion cell diseases.

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**ERG Clinical Applications**

- Differentiate retinal and optic nerve disorders
- Inconsistent or borderline test results (Patient symptoms or test results are equivocal)
- Diagnose and manage treatment efficacy of subclinical ophthalmic disorders:
  - glaucoma
  - age-related macular degeneration (AMD)
  - diabetic edema, diabetic retinopathy
  - Toxicity/plaquenil

"The pERG arises largely in the ganglion cells, driven by the photoreceptors and corresponding retinal cells. Since the pERG (in contrast to the flash ERG) is a local response from the area covered by the retinal stimulus image, it can be used as a sensitive indicator of dysfunction within the macular region and it reflects the integrity of the optics, photoreceptors, bipolar cells and retinal ganglion cells."
At higher temporal frequencies, that is, above 10 rps (5 Hz), the successive waveforms overlap and a “steady-state” PEG is evoked."

Per NIH and Bascom-Palmer:

In patients who are glaucoma suspects, PERG signal anticipates an equivalent loss of OCT signal by several years (as many as 8 years).

DOI: 10.1167/iovs.12-11026

Pattern ERG- Steady State

- **Concentric Stimulus Fields** - Protocol driven test designed for objective, functional study of focal disease (drug toxicity, diabetic edema, AMD)

- **Contrast Sensitivity** - Protocol driven test designed for objective, functional study of diffuse disease (glaucoma, diabetic retinopathy, etc)

Concentric Stimulus Field pERG

Information affecting the central or paracentral area of the macula and ganglion cells: AMD, Plaquenil, Diabetic Edema

Waveforms in Phase = normal

Testing Protocols: Concentric Stimulus Fields

- Stimulus delivered at 15 rps/second
- BCVA Patient should be properly refracted for 24°.
- 24° testing distance
- 80% contrast
- Right Eye (OD) then Left Eye (OS)
  - 25 seconds at 24°
  - 25 seconds at 16°
Testing Protocols: 
Contrast Sensitivity

- Stimulus presented at 15 flips/second
- BCVA
  - Patient should be properly refracted for 24
d- Testing distance
- Right Eye (OD) then Left Eye (OS)
  - 25 seconds at High Contrast (Hc)
  - 25 seconds at Low Contrast (Lc)

Normal PERG Response

3 Quick Steps To Report Interpretation

- Signal Quality – Look for a green signal
- Sinusoidal Peaks – Look for 3 humps
- Magnitude, MagnitudeD and MagD/Mag Ratio are colorized.
  - Green indicates within normal limits
  - Yellow indicates values are borderline
  - Red indicates outside normal limits

PERG Report – Data Table

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OD 30'</th>
<th>OD 90'</th>
<th>OD 15'</th>
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<tbody>
<tr>
<td>Magnitude (μV)</td>
<td>1.34</td>
<td>0.98</td>
<td>0.81</td>
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<tr>
<td>MagnitudeD</td>
<td>1.25</td>
<td>0.89</td>
<td>0.71</td>
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<tr>
<td>SNR (μV)</td>
<td>7.2</td>
<td>4.2</td>
<td>3.1</td>
</tr>
<tr>
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Magnitude (μV) is defined as the strength of the patient’s response at a reversal rate of 15 reversals per second.

Larger magnitudes are typically generated from normal eyes. Smaller magnitudes typically indicate pathology.

As the contrast level drops or the stimulus size decreases, the magnitude will typically decrease.

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MagD/Mag Ratio is the most repeatable measurement test over test. The closer the ratio is to 1.0, the lower the phase variability throughout the test, and the healthier the patient’s response. Variability in phase may indicate pathology.

MagD/Mag ratio can be used to monitor patients over time.

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SNR - Signal to Noise Ratio shows how strong the signal is at 15Hz compared to noise at 15Hz. Larger numbers indicate stronger PERG signals compared to the noise.

SNR values like 5, 15, >20 show strong PERG response. Numbers less than 2 are typical of a weak response.
Artifacts are caused by blinking or patient movement. They are detected and counted. A high number of artifacts will affect the amount of data that can be analyzed.

The goal is to have a low number of artifacts. The patient should be comfortable and blink when necessary, but not excessively. The goal is less than 10. If test results show Artifacts greater than 10, the test should be repeated.

PERG - Summary

PERG is an objective, functional test on the retina that can discriminate between healthy and diseased eyes.

- Differentiate retinal and optic nerve disorders
  - Abnormal VEP to isolate dysfunction 794.13
  - Retinal 362.xx and Optic Nerve 377.xx concerns
- Questionable, inconsistent or borderline test results (Patient symptoms or test results are equivocal)
  - Visual Disturbances 368.xx
  - Retinal Disorders 362.xx
  - Optic Nerve function 377.xx
- Diagnose and manage treatment efficacy of subclinical ophthalmic disorders:
  - Glaucoma 365.xx
  - Age-related macular degeneration (AMD) 362.30
  - Diabetic retinopathy - Retinopathy 248.xx and 362.xx
  - Toxicity from drug use/Apothecary 380.xx

The Case of the Missing Exam

WC, a 33 year old Caucasian male was seen for a second opinion consultation regarding a diagnosis of advanced glaucoma in one eye.

History was negative for medical treatment in fact until the initial eye exam the patient had never seen a doctor since early high school.

Patient was asymptomatic other than distance blur which precipitated the original eye exam

Denies trauma, Fam Hx, medications

Currently on TZ 1/0

Case of the Missing Exam

Clinical Assessment:
Vacc: 20/20 (OD/OS)
To: 9/14 4/3:30
HFA II: As shown
Ext: 3/3/2+/ +MG OD
SLE: Unremarkable
Pach: 56/572
Tora: 8.4/ 14.7
DFE: As shown
The Case of the Missing Exam

- **Clinical decision?**
- What do you recommend?
- Same drug?
- Change drug?
- No tx!
The Case of the Missing Exam

MRI report:

**Case 1: Glaucoma Suspect**

- Inconsistent baseline test results

- Banitt et al. Progressive Loss of Retinal Ganglion Cell Function Precedes Structural Loss by Several Years in Glaucoma Suspects. IOVS, March 2013, Vol. 54, No. 3 (From the Bascom Palmer Eye Institute, supported by Grant National Institutes of Health—National Eye Institute [NEI], NIH Center Grant, and Research to Prevent Blindness)

- Visual fields are full, HRT normal

**Case 2: Diabetic Retinopathy**

- Subclinical management required for patient compliance

- Patient has Kruckenbeld spindles and IOP in 20's, therefore, is a glaucoma suspect.

- PERG shows borderline results. This defines a higher level of risk over time and the patient should be followed on a more intensive basis.
Case 2: Diabetic Retinopathy

- OCT OD
- OCT OS

Case 3: ERM

- OCT OD
- OCT OS

Case 2: Diabetic Retinopathy – ERG

- OCT OD
- OCT OS

Case 3: ERM – subclinical management for appropriate treatment

Patient Work-up

- Age: 60
- Weight: 175Lb
- Complain/Symptoms: Floaters
- Family History: None
- Height: 5f
- IOP (mmHg) OD: 15
- IOP (mmHg) OS: 16
- Refraction OD: +2.00 -1.00 x 155 +2.75
- Refraction OS: +2.25 -2.00 x 180 +2.75
- VCVA OD: 20/25
- VCVA OS: 20/30
- Preliminary Diagnosis: Hypertension, Cataract, Epiretinal Membrane (ERM)
Case 3: ERM - ERG

When used judiciously to improve visual function, medically necessary.

VEP CPT 95930
- For subclinical optic nerve concerns (beneath the surface of clinical detection)
  - 377 (optic nerve/pathway disorders)
  - 368 (questionable vision)
- Systemic or Traumatic manifestations that affect vision
  - 368 (visual disturbances) or other signs and symptoms or concerns from:
    - Neurological, TBI, Infectious, Infiltrative, Degenerative,

ERG CPT 92275
- For subclinical retinal concerns (beneath the surface of clinical detection)
  - 365.0X Glaucoma suspects
  - 377 (optic nerve/pathway disorders)
  - 365.1X and greater, confirmed glaucoma (mild to moderate stage)
  - 362 Retina (DR), Macula (AMD) and toxicity concerns

Can I use both tests on the same day?
- Both tests seen used to locate dysfunction – is it retinal (ERG) or retrobulbar (VEP) - optic nerve to visual cortex?
- Always requires documentation of medical necessity and impact on care
- May be performed same day as other tests, NO Correct Coding Initiatives
- Select the most appropriate ICD for the chief reason for the test – different reasons for different tests

Visual Electrophysiology is accepted as an additional testing method when more in-depth measures of visual function are required for diagnosis.