The ABCs of VEPs

Disclosure: Jerome Sherman has received honorarium from Optos, Meditec, Philips, Ariniis, Topcon, Optivue, Dioppsys, Zeiss, Artic, Eye Solutions and Quantal and received support for Retina Revealed www.retinarevealed.com from all and also from Heidelberg and DGH.

Historical Perspective(s)
As I Experienced it

- I was the graduate student of the late Bill Ludlam in 1970
- First VEP articles published at that time
- Homemade systems - 14 different devices – combined
- Faraday Cage
- Removed metal-jewelry etc
- Occasionally did VEPs on infants while breast feeding
- Many difficult syndromic kids – several violent
- Did special for NBC news with Dr Frank Field on adorable young girl with Downs syndrome
- TV special resulted in great PR for SUNY

VEP & ERG for the Office: How New Technology Can Impact Your Practice
1970 vs now!

Presented By:
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MAIN INDICATIONS
- Glaucoma
- Multiple Sclerosis
- Ischemic Optic Neuropathy
- Traumatic Brain Injury
- Amblyopia
- Other Neuropathies
- Hysteria or Malinger
ging
- Blurred or reduced vision

Visual Evoked Potential (VEP)

Objective measurement of the function of entire vision system;
No verbal response or "button pushing" like visual field tests
Eye stimulation by a checkerboard pattern elicits a ganglion cell response known as PERG.

PERG is an accurate and objective indicator of ganglion cell and retinal function (ISCEV).

PERG can detect retinal dysfunction (DIET) before structural tests (Parisi et al).

BEYOND OPHTHALMOSCOPY

Clinical Electrophysiology of Vision (CEV)

Pattern ERG
Flash ERG

Electrical activity of the retina

Pattern ERG = PERG

Main Indications
- Glaucoma
- Maculopathies

Can also help the clinician differentiate between retinal and optic nerve disorders when used in conjunction with Visual Evoked Potential (VEP).

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


Per NIH and Bascom-Palmer

Referred by Nancy Glassman OD for VEPs

Referred by Nancy Glassman OD for VEPs
**STABLE STATE PERG**

Higher temporal frequencies - 15 reversals per second (rps), 7.5 Hz. Successive waveforms overlap and a “steady-state” PERG is evoked.

**PERG Sensors**

**Structure**

- Ophthalmoscopy
- Fundus photography
- Panoramic Imaging (Optos)
- Fluorescein Angiography
- B- scan ultrasound
- OCT III, SD OCT
- GCC
- GDx VCC & HRT
- FAF - Fundus autofluorescence

**Function**

- Visual Acuity
- Pupils
- Fields, PHP, MAIA
- Color vision
- Contrast Sensitivity
- Rabin Col/Contrast
- ERGs and EOGs
- Pattern and mf ERGs and pERGs
- VEPS (pattern & flash)

**True or False:**

If the fundus looks normal with an ophthalmoscope, the retina and optic nerve are normal.

**FALSE!**
Sensitivity: the proportion of actual positives which are correctly identified as such.
- e.g., the percentage of sick people who are correctly identified as having the condition

Specificity: the proportion of negatives which are correctly identified as such.
- e.g., the percentage of healthy people who are correctly identified as not having the condition

Normal Subjects:
- Sensitivity: 90%
- Specificity: 86%

Retinal and/or optic nerve disease:
- Sensitivity: 95.5%
- Specificity: 90.0%

Retinal Pathology:
- Sensitivity: 96%

Optic Nerve Pathology:
- Sensitivity: 99%

**SPECIFICITY & SENSITIVITY**

**VISUAL EVOKED POTENTIAL ASSESSMENT OF NEURO-VISUAL FUNCTION**

**ANATOMY**
- Photoreceptor
- Bipolar
- Ganglion
- Ganglion cell axon
- Relay neuron
- Relay neurons axon
- Visual cortex neuron

**BEYOND OPHTHALMOSCOPY**

**Psychophysics of vision**
- Contrast Sensitivity Test

Dx of Optic Neuropathies: Beyond the Basics

Case 50 – GCC, VEP and RAPDx
A 29-year-old white female presented complaining of blurred vision in her right eye since having a sinus infection about 4 weeks earlier. The sinus infection resolved but the vision in the right eye was reported as "off" when compared to her left eye. General health history was unremarkable. Best corrected VA with low minus was 20/20 OD and 20/20 OS.

The pupils, observed by several different clinicians, were judged as normal and a RAPD was not observed. The macula and discs were unremarkable in each eye. Color vision with PIP yielded 11/11 correct in each eye but the patient commented that the test was more difficult with the right eye.

Comparison of the right and left maculas and discs of each eye failed to reveal an explanation for her symptoms.

Standard threshold fields were normal in each eye.
**Case 1: Optovue Wellness OU Exam**

The Wellness exam was performed. This test has recently been reported to have 91% sensitivity and 95% specificity for glaucoma.

**Case 2: ZEISS Humphrey 30-2 Visual Fields OU**

The GCC asymmetry is not reflected in the central threshold visual fields. Learn more about GCC... (link)

**Case 1: Diopsys™ Nova-DN OU**

In our 23 year patient with blurred vision in her right eye, the VDN are normal in amplitude but delayed in the right eye. Under high contrast conditions, the VEP F200 latency is delayed by 33 msec in the right eye when compared to the normal latency in the left eye. Under standard Nova-DN conditions, the entire pattern reversal stimulus contains 52x52 checker.

**Visual Evoked Potentials (VEPs)**

With VEP's, the patient is treated as a "black box" and the patient looks at objects (usually black and white) that pattern reversal, which checks black and black checks visible in a specific visual area. The pattern reversed stimuli presents a change across the central retina and this change is transmitted via the optic nerve and visual pathway to the occipital lobe. The response (measured from the back of the head with a surface electrode) has either stimulus, one's reference and the other a ground are also used.)

**VISUAL EVOKED POTENTIAL**

**ASSESSMENT OF NEURO-VISUAL FUNCTION**
Phototransduction
Conversion of light into electricity

Exemplary normal VEPs

Interpreting the VEP:
Each pattern reversal of the black and white checkerboard results in a change in retinal stimulation, followed by the transmission of action potentials to the occipital cortex.

The pattern reversal occurs at time 0, and the first negative wave (below the baseline) is detected at about 70 ms after the change in stimulation.

This is followed by the first major positive wave which is termed the P100, after the stimulus trigger. The size or amplitude of the response is measured from the trough of the N70 to the peak of the P100.
VISUAL EVOKED POTENTIAL
ASSESSMENT OF NEURO-VISUAL FUNCTION

Psychophysics of vision

Visual Acuity Test

In our 29 yo patient with blurred vision in her right eye, the VEPs are normal in amplitude but delayed in the right eye. Under high contrast conditions, the VEP P100 latency is delayed by 33 msec in the right eye when compared to the normal latency in the left eye. (Under standard Nova-DN conditions, the entire pattern reversal stimulus contains 32x32 checks.)

The VEPs above were obtained to smaller checks at high contrast (pattern reversal stimulus contains 32x32 checks). Under these conditions, the VEP P100 wave was delayed to 160 msec which is nearly a 50 msec difference when compared to the left eye. Such large delays are known to occur because of demyelination, often in Multiple Sclerosis (MS).

Note the obvious difference in latency between the RE and LE when the VEPs are directly compared.

Although a RAPD was not demonstrated clinically, the GCC revealed loss of ganglion cells in the right eye within one month of visual symptoms in the right eye. The VEP was quite delayed in the right eye in spite of normal visual fields and normal pupils. Similarly, the RAPDx was grossly abnormal in the right eye in spite of the normal pupils observed clinically.

Based upon the previous results, an MRI of the brain was recommended. The MRI revealed numerous white signal abnormalities in the periventricular and juxtacortical white matter consistent with demyelination and multiple sclerosis. The patient has now obtained consultation with two neurologists and various treatment options are presently being considered.

40 yo white female with recent Dx of MS
VA 20/50 R  20/30 L
Neurologist wants VEP baseline prior to beginning new Rx

(It has been previously published by IBW that patients with Parkinsons Disease have VEP delays which improve with successful treatment with L dopa related drugs)
SUNY ORS

- 64 year-old WM seen by a local optometrist in NYC on July 19, 2011.
- Pt. BC VA OU was 20/20 and his IOPs @ 4pm on July 19, 2011 were 24 in OD and 16 in OS.
- IOPs were taken on another day, July 25, 2011 @ 10am OD was 18 and OS 13.
- O.D. did several VF on the OD and noted that Pt. had VF defects superiorly and inferiorly. OS was WNL.
- Pt. then referred to University Eye Center at SUNY College of Optometry where Dr. has requested further testing.
- Procedures done at SUNY: GDx, OCT, HRT, Pachymetry, VEP, Humphrey Visual Field, and ORA.
- IOPs done on December 15, 2011 @ 6pm OD was 34 and OS was 22.
Visual Field Results: OD

Most info in single print-out

In the GDx printout, red-orange-yellow above and below the disc indicates a normally thick NFL. Blue-purple indicates a relatively attenuated NFL, which normal nasally and temporally, but not superiorly or inferriorly.

For 25 years a patient’s glaucoma went undetected!!!

GDx has been a very reliable yet new instrument that takes literally 2 minutes to demonstrate an abnormal NFL and provide convincing evidence that glaucoma is indeed present in a patient.
The Reichert Ocular Response Analyzer provides a new measurement of corneal tissue properties called Corneal Hysteresis (CH) that is a result of viscous damping in the corneal tissue.

**ASSESSMENT OF NEURO-VISUAL FUNCTION**

Eye stimulation by a checkerboard pattern elicits a ganglion cell response known as pERG.

pERG is an accurate and objective indicator of ganglion cell and macular function.

(pERG) can detect retinal dysfunction (DRH) before structural tests.

(Parisi et al.)
Case Review
Physiological or Pathological cupping?

Reason for test:
C/D .8 OU
T max = 22 OU

Patient Work-up

Gender Female
Age 38
Ethnicity Asian

Family History
Mom reported to have Glaucoma

Pachymetry
OD 530.00
OS 535.00

Date of Exam
Exam 1
Exam 2
Exam 3

IOP (mmHg)
OD
23
23
23

OS
20
23
22

BCVA
OD
20/20
20/20
20/20

OS
20/20
20/20
20/20

Refraction
OD and OS
-1.50 OU
-1.50 OU
-1.50 OU

Preliminary Diagnosis
Glaucoma suspect

Cupping without Glaucoma?

MC 62 y/o white female
subjective VAs
difficult to access

Visual Fields:
Minor reduction but no consistent loss OU

OD Color
OS Color

ResMax
-6.00 OU
-6.00 OU
**Case 3:** A 7 year-old WM with bilateral optic disc pallor, was previously diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) which perhaps explained the difficulty in examining this young patient. A female resident who spent considerable time with this youngster was able to connect his left 20/20 OD and OU. Optosimetry revealed temporal pallor, but it was unclear whether this was phlebitic or pathologic. Digital stereo inspect revealed soft glotes.

**Case 3:** A 7 year-old WM was evaluated because of possible reduction of VA and possible disc pallor. He was previously diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) which perhaps explained the difficulty in examining this young patient. A female resident who spent considerable time with this youngster was able to connect his left 20/20 OD and OU. Optosimetry revealed temporal pallor, but it was unclear whether this was phlebitic or pathologic. Digital stereo inspect revealed soft glotes.

**Case 1:** 3.5 year old child was referred for consultation because a trial of direct patching did not improve visual acuity in his "amblyopic" right eye. BSV was 20/20 OD and 20/20 with 1.75 -1.75 x 180 OD and 1.75 -1.75 x 180 OS. No mom reports she first noticed the right eye turn out at about age 2. Because of reports of hypometric and a limited attention span, VEP were obtained prior to any other testing. Note that with no significant anisometropia or constant unilateral strabismus, the diagnosis of amblyopia is not supported.
Can the occipital lobe of the brain, which functions best with synchronous visual input, process this asynchronous visual input? More about this later.

The VEPs are normal in Amplitude in the right eye under both Low Contrast (Lc) and High Contrast (Hc) conditions but the Latency is prolonged under both conditions as indicated by the two red vertical bars.

In the left eye, the VEPs are within normal limits with regards to both Amplitude and Latency as indicated by the 4 green vertical bars.

In the Parameter table, note that the delay between the two eyes is 28 msec under Lc and 24 msec under Hc conditions.

Under green separation, the normal retinal nerve fiber layer (RNFL) exhibits white striations, most easily seen in the superior temporal and inferior temporal arcades. Although the RNFL appears normal in the OS, it is virtually invisible in the OD.

Case 1: Topcon 3D OCT Scan OD and LE showing a poorly defined PIL relative to the LE and thinner RNFL near the disc RE vs LE.

Although the retinal pigment epithelium (RPE) is only a single layer of cells, it appears as two reflective layers with a dark zone in between on high definition OCT scans. The "inner reflection" has been referred to by some authors as the outer segment-RPE interdigitation (OS/RPE) or Verhoeff’s membrane. The outer reflection is the RPE/Bruch’s membrane complex (RPE/BBM).

In this case, note the difference in latency of the P100 between the right and left eye. A 24 msec delay is present under the High Contrast condition.
Histological Section as Compared to the OCT Image

Although the photoreceptor integrity line, or the PIL, defined as the junction between the inner and outer segments is barely visible in most histological sections, it is highly prominent in normal SD OCT. The PIL, as shown above, should be continuous throughout the entire scan in normal eyes. The PIL is considered by some as a marker for that due to the difference in the index of reflection of the inner and outer segments but the artifact is remarkably useful in SD OCT interpretation.

Case 1: Optovue iVue OCT OD

Vise Vertical scan through figure 1, showing PIL difference. Note the difference in brightness/visibility of the PIL between the right and left eye. The PIL is present but poorly defined in the right eye. This difference suggests structural photoreceptor impairment OD.

Binoctual measurement in a 5-year-old revealed suppression of the right eye under all conditions tested. The delay due to the asynchronous visual input arising at the occipital pole. Although the right and left eye had the same latency, perhaps the binocular critical can be estimated with an improvement in binocular vision.

We demonstrated previously that excised density filters result in VPs asking. This knowledge can be used to determine the better eyes in order to slow the patient to match the VP latency of the "amblyopic" eye.

Case 1: Topcon 3D DU Fundus Photos OD

Diagnosis: The VA reduction appears to be due to a central reduction in both photoreceptors and in the fovea of the right eye. The normal appearance of the disc in the right eye is likely congenital as well and related to the central reduction. Histologically, any asymmetry is superimposed upon the structural abnormality. The abnormal appearance may be detected due to the difference in the size/shape, but what is present here is a difference in the lens density filter in front of the lens that displays synchronous visual input to the occipital pole from both eyes.

VEP Prognostic Guidelines: Pattern VEPs in "amblyopic" eyes are sometimes normal in amplitude, waveforms and latency phase with the VEP from the fellow eye. As a general rule, the latency VEP better the photoplethysmography. Such patients should be carefully observed and may have other similar cases respond to patching and vision training. They may have any other other sensory abnormality in the brain, which can be later developed.

The delay may be due to a senso-receptor abnormality or a delay in secondary processing. Single fiber and electroretinography are normally within normal limits for all VEP test cases. In contrast, other cases reveal that the pattern VEPs is flat with one-chance and wave form is greater than stimulation. These patients do not have amblyopia but may have a sensory disorder such as isomorphic in the brain.

Therefore, this patient may have a "light" sense, patients with normal VEPs with normal visual acuity and normal visual acuity for the "amblyopic" eye. Such cases can be highlighted in an future.

This case here of our 5-year-old lies somewhere in between these two extremes.

Case 1: Diopsys Nova-DN DU

Neutral Density Filter.

VPs and VFs in Amblyopia

- Amblyopia is a disease of light sense, not
- Visual fields are essentially normal in amblyopia
- Mild central desensitivity may be noted
- Increased in fixation losses may be noted
- Flash VEPs are normal in amblyopia
- If not, amblyopia is not the correct Dx
Case 3: A 31yo Hispanic male had an accident at work 6 months earlier and reports that a nail gun entered his right eye. His symptoms were lessened superiorly and then resolved. A fluorescein coronary developed which was then removed. Since the accident BCVA is light perception OD and 20/20-0 OS. External exam revealed superior corneal sutures (as seen above) and an iritis OD. Keratometry demonstrated irregular limits secondary to the trauma and corneal sutures OD only. Ophthalmoscopy was within normal limits OD.

The fundus of the right eye appears normal and is essentially a mirror image of the fundus of the normal left eye.

The GCC “green donut” looks completely normal in the right eye. The thickness measurements are all within normal limits and symmetric with the normal left eye.

The wave form is better formed in the left eye (compare the high contrast waves) than in the right eye but the relative reduction in amplitude in the OD is likely due to the corneal irregularity. In addition, the patient tended to look away from the stimulus when testing the right eye.

The pattern VEP is normal in amplitude and in latency under the standard conditions tested with the Diopsys NOVA-On.

The waveform of one eye is triphasic with superior fixation on a dot, rather than a stimulus, and no corresponding VEP is seen in the other eye. Such a pattern VEP is the result of an organic or neural disorder. Since the subjective VA is light perception there is a discrepancy between the objective VEP and the subjective VA. This is not typical of a retinal or neural “figure” pattern but quite typical of a “functional” VEP. This may be an enhancing or de-enhancing synonymous condition. Additional questioning revealed that the patient was attempting to collect workman’s compensation and did not want to report his previous employment. Di: Malingering.

VEPs were repeated under other conditions: smaller test size (2 disk rather than 10 Hz) and a larger number of signal averages (10 pattern reversals rather than 1). Each pattern reversal is 2 sec and hence this test took 60 sec/eye rather than 15 sec/eye. A VEP is clearly present in both the right and the left eye and the latencies are not dramatically different. The reduction in amplitude in the right eye is most likely due to the imperfect imaging of the chias onto the retina because of the corneal distortion secondary to the trauma, the surgery and the sutures.
Case 4: A 31 yo WF was referred for evaluation of visual sequelae due to acquired brain injury incurred 4 years earlier. She was diagnosed with anoxic encephalopathy and has since remained perceptually and cognitively impaired. Her pre-incident memory is very spotty. BCVA is 20/100 OD and 20/100 OS with a refractive error of -5.00. External examination revealed 1+ RAPD OS. The optic nerves appeared normal with probable physiologic temporal pallor. The VEP under standard Diopsys NOVA-EN conditions is normal as to waveform, amplitude, and latency under both low and high contrast conditions in each eye. Such VEPs are commensurate with normal retina, optic nerve and visual pathway function.

The VEPs are normal under other conditions as well. Here very small checks (32x32 checkerboard) were pattern reversed once per second for 60 sec in each eye. Such VEPs suggest normal corrected VA in each eye.

**VEPs and VFs in Amblyopia**

- Amblyopia is a disease of form sense, not light sense
- Visual fields are essentially normal in amblyopia
  - except for monocular nasal field cuts in high angle esotropia
  - Mild central desensitivity may be noted
  - Increase in fixation losses may be noted
- Flash VEPs are normal in amblyopia
- If not, amblyopia is not the correct Dx

**Beyond Ophthalmoscopy**

Other Electrophysiological tests

- Electroretinogram
- Multifocal Electroretinogram
- Pattern Electroretinogram
- Electrosclerogram
- Multifocal Visual Evoked Potential

**VisuAl Evoked Potential Assessment of Neuro-Visual Function**

<table>
<thead>
<tr>
<th>ERG</th>
<th>mERG</th>
<th>PERG</th>
<th>EOG</th>
<th>mVEP</th>
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Incorporating Vox 10/20 and HealthCloud exam brings the comprehensive eye exam to a whole new level.
Although the photoreceptor integrity line, or the PIL (defined as the junction between the inner and outer segments) is barely visible in most histological sections, it is highly prominent in normal SD OCT. The PIL, as shown above, should be continuous throughout the entire scan in normal eyes. The PIL is considered by some as a mere artifact that is due to the difference in the index of refraction of the inner and outer segments but this artifact is remarkably useful in SD OCT interpretation. The PIL as Revealed by SD OCT is available at: http://www.lulu.com

Although the retinal pigment epithelium (RPE) is only a single layer of cells, it appears as two reflective layers with a dark zone in between on high-definition OCT scans. The "inner reflection" has been referred to by some authors as the outer segment-RPE interdigitation (OS/RPE) or Verhoeff's membrane. The outer reflection is the RPE/Bruch's membrane complex (RPE/Br). Note the two reflections from the RPE complex are only visible on high-definition scans. On lower resolution OCT scans the RPE generally appears as one solid thick band.
Case: Laurence-Moon Bardet-Biedl

- Polydactyly – both patients had 24 digits at birth. Scars are visible on the hands where digits have been removed. Additional digits on the feet are still intact.

Diagnosis

• Probable Laurence-Moon or Bardet-Biedl or LMBB syndrome and not autism!
• Genetic testing for the BBS1 gene is now available (Carver Nonprofit Genetic Testing Lab at www.carverlab.org).

Historical Perspective(s) As I Experienced it

Hysteria- normal VEP
(usually not on a conscious basis)
Grand Hysteria or Multiple Personalities
(now known as Dissociative Personality Disorder)

GEM: Story to be told that you will never forget. A 2 minute test changed the life of this patient.

Historical Perspective(s) As I Experienced it

• Exemplary case of Malingering (often a monetary goal)

• Dental hygienist with large engagement ring and great nails. History of dental syringe bursting causing a large sub-conjunctival hemorrhage and blindness in one eye.

GEM: story to be told that you will never forget!
PERG - Summary

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

Indications:
- Glaucoma
- Maculopathies

Visual Assessment

Dynamic Visual Function Assessment

Perimetric Testing

Macular Function

Flash ERG

Macular Function

Flash Stimulation
Ganzfeld Cataract


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**Case: FA72**

Age (years): 72
Gender: Female
Complaint: Blurry vision (OS)
Personal History: Thyroid disease, LASIK
Family History: None
Allergies: No known allergies
Uncorrected VA OD: 20/25
Uncorrected VA OS: 20/40
Refraction OD: +0.25
Refraction OS: -1.25
BCVA OD: 20/25
BCVA OS: 20/40

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**Case: FA72**

IOP OD (mmHg): 11
IOP OS (mmHg): 17
Pupil OD: PERRL, negative APD
Pupil OS: PERRL, negative APD
Anterior Segment OD: IOL, trace PCO
Anterior Segment OS: 2+ NS, Cortical 2+
Fundus Exam OD: Normal, CD 0.5
Fundus Exam OS: Normal, CD 0.4
Diagnosis: Cataract (OS)
**Age (years):** 72

**Gender:** Female

**Complaint:** Blurry vision, OD>OS

**Personal History:** Thyroid disease, Retinal detachment (OS)

**Family History:** Hypertension

**Allergies:** No known allergies

**Uncorrected VA OD:** 20/50

**Uncorrected VA OS:** 20/40

**Refraction OD:** +2.25

**Refraction OS:** +2.25

**BCVA OD:** 20/50

**BCVA OS:** 20/25

**IOP OD (mmHg):** 14

**IOP OS (mmHg):** 13

**Pupil OD:** PERRL, negative APD

**Pupil OS:** PERRL, negative APD

**Anterior Segment OD:** 2+ NS

**Anterior Segment OS:** 2+ PED

**Fundus Exam OD:** Normal

**Fundus Exam OS:** Normal

**Diagnosis:** Cataract (OU), Retinal detachment (OS)

**Clinical Electrophysiology**
Thank you!

Questions?