Clinical applications

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Conflict of Interest

None
Outline

Anatomy
Physiology
Methods
Technical factors influencing results
Clinical Applications
Some examples
Conclusions
Background

Adrian and Matthews (Brain, 1934), “The Berger rhythm: potential changes from the occipital lobes in man”
First described miniature potentials of the occipital cortex when a patient was exposed to visual stimuli.

Halliday et al (Lancet, 1972), first to applied clinically pattern reversal VEPs in the diagnosis of patients of optic neuritis. Nowadays, PRVEP are an objective electrophysiological method to diagnose and monitor numerous ophthalmological and neurological diseases. They also are an objective way of study visual acuity and visual field in the assessment of cases having suspected multiple sclerosis (MS).

Flash VEP are useful in children which do not cooperate for the neurologic evaluation, and in cases of aggravation of ophthalmologic pathologies.

PVEPs useful to evaluate functionality of visual pathway, monitor diseases of the retina, optic nerve, visual tract, optical radiation and visual cortex.

Most of the cases in clinical practice, however, concentrate in pathologies of the Optic Nerve (≈ 90%).
Optic Nerve

a. Intraocular 1mm
b. Intraorbital 25mm
c. Intracanalicular 9mm
d. Intracranial 12-16mm
Contralateral optic radiations
Layers 1,4,6

Ipsilateral optic radiations
Layers 2,3,5
Occipital Cortex

Primary Visual Cortex (V1)

Superior Retina → Cuneus
Inferior Retina → Lingual Gyrus
Secondary Visual Cortex (V2)

**Dorsal Bundle:** Posterior parietal cortex: Spatial and movement of objects (*where*)

**Ventral Bundle:** Inferotemporal cortex: Recognize faces, shapes, size, colors (*what*)
**Visual Pathway**

**Temporal Retina:** fibers of the Optic Nerve (ON) are uncrossed (45%)

**Nasal Retina:** fibers of the ON decussate at the optic chiasma (55%)

**Visual Fields:**

Temporal Field ---- Projects to the Nasal Retina
Nasal Field --------- Projects to the Temporal Retina
Principles of PRVEP

Pattern reversal VEP is a diagnostic tool, that examine conduction of the visual pathway.

Checkerboard pattern reversal is the most widely used stimulus because of its relative simplicity and reliability.

Checks help to explore the function of the striate cortex (area 17) because confined spatial frequency analyzers are likely present there.
Types of Visual Stimulation

Checkerboard Pattern Reversal. Full, hemi field, quadrant

Googles (diffuse light, flash)
Shape of the VEPs

Absolute Latencies (ms)
N75, P100, N145

Amplitudes (µV)
N75-P100
P100-N145
Methods

70-100 cm from the screen
Constant visual fixation to the center of the screen
RR <4 Hz
Smaller check sizes stimulate fovea. Foveal fibers are the fastest fibers, thus latencies shorten
Stimulation with larger checks, stimulates peripheral fibers which are slower than foveal fibers

Latency

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<td>30°</td>
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<tr>
<td>60°</td>
<td>107.2</td>
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<td>120°</td>
<td>104.42</td>
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<tr>
<td>30°</td>
<td>147.52</td>
</tr>
<tr>
<td>60°</td>
<td>145.25</td>
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<td>60°</td>
<td>11.68</td>
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<tr>
<td>120°</td>
<td>11.91</td>
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<td>30°</td>
<td>11.89</td>
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<td>60°</td>
<td>12.33</td>
</tr>
<tr>
<td>120°</td>
<td>12.84</td>
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Other types of Visual Stimulation

Multifocal visual evoked potentials

Pattern reversal Steady State visual evoked potentials
The Queen Square System is superior to the IFCN because LO and RO are farther than O1, O2, thus larger signal.
As with any Evoked Potentials study, keep impedances below 5 KΩ
Settings for PRVEP

✓ Patient Position: Seated comfortably
✓ Dim light room
✓ Screen 70-100 cm in front of the eyes
✓ Fix to the center of the screen (specially in hemifield stimulation)
✓ Correct visual acuity with patient lenses (in case of using)
✓ Monocular stimulation by covering non stimulating eye
✓ Be sure the patient remains fully alert
✓ In hemi visual stimulation, must focus in central spot
Factors affecting latency and amplitude

1. Sex: women have shorter latencies than males
2. Head size: the larger head the size, the longer the latency of the P100
3. Pupillary size: do not perform VEPs with dilated or constricted pupils (avoid anticholinergic or sympathetic substances)
4. Visual Acuity: always correct refraction errors
Recording and Stimulus

- **Filters**  LFF: 0.2-1.0 Hz /HFF: 200-300 Hz

- **Sweep** 20-25ms/div, **Sensitivity** 5-10 µV/div

- **Average** 150-200 responses

- Polarity agreement not standardized

- **Stim rate** 1.3-2.7 (avoid integer of 60 Hz). Higher rates may increase latencies

- **Brightness contrast** = >0.5 (Lmax-Lmin/Lmax+Lmin)

  L: Luminance measured by a photometer
How display monitors affects VEP latencies

- **CRT:** Cathode ray tube refreshes almost instantaneously.

- **LCDs:** the fastest refreshes at 2 ms, slower than CRT, despite better resolution.

- The slower the refreshing time, the longer the latency of VEPs. Some LCD refreshes at 30 ms and cause extreme P100 latency prolongation.

- Normative values, should be done with only one display. In case of upgrade monitors, run normative data again.
VEP analysis

• Wave recognition: N70, P100, N145 in midline and parasagittal electrodes

• N105 in MF-AU

• Latencies P100: 95-115 ms Interocular latency differences < 8 ms

• Amplitude N70, P100 and N145 (P100 Interocular amplitude difference < 2 SD)

• Shape “V” and “W”
Montages and shape of waves

Channel 1: Left occipital to midfrontal = LO-MF
Channel 2: Midoccipital to midfrontal = MO-MF
Channel 3: Right occipital to midfrontal = RO-MF
Channel 4: Midfrontal to ear/mastoid = MF-AI

It should be noted that up to 15% of cases, N100 may be absent in normal subjects.
Influence of head size/Sex VEP Latencies

Gregori et al, showed a clear correlation between head size and P100 Latency. ON the other hand, sex differences had not a strong correlation.
Factors affecting VEP responses

- **Age**: Age decreases flicker sensitivity producing increments in latencies of Steady state VEPs. These age-related changes affect the magnocellular (M) but not the parvocellular (P) pathways, as shown by Brown, A et al*

* doi.org/10.3389/fnagi.2018.00430
INTERPRETATION

- Latency P100
- → Oz (MO) - Fz
- → At the maximal *plateau*

<table>
<thead>
<tr>
<th>Age</th>
<th>Female</th>
<th>Male</th>
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<tbody>
<tr>
<td>&lt; 60 Y</td>
<td>&lt;115ms</td>
<td>&lt;120ms</td>
</tr>
<tr>
<td>≥ 60 Y</td>
<td>&lt;120ms</td>
<td>&lt;125ms</td>
</tr>
<tr>
<td>Interocular latency</td>
<td>&lt;10 ms</td>
<td></td>
</tr>
<tr>
<td>Side to side amplitude</td>
<td>&lt;50%</td>
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Mayo Clinic Normative P100 Values
When using scalp-scalp derivations, with Oz-Fz montage, both electrodes are active. Since Fz and Oz have signals, they are related to but not perfectly synchronous. This can result in a shift in the apparent latency of the P100 or result in a less well-defined or 'W' wave form. Thus, the importance to use frontal montages as well.
Paradoxical Responses

Because of the direction of the P100 dipole, the projection of the activated cortex, is reflected better in the contralateral electrode.
Specifics for Abnormalities

1) **Latency prolongation of P100**
   - Monocular: pre-chiasmatic
   - Binocular: pre-chiasmatic, chiasmatic, post-chiasmatic or technical error

2) **Amplitude**
   - Monocular: pre-chiasmatic or technical error
   - Binocular: pre-chiasmatic, chiasmatic, post-chiasmatic or technical error

3) **Topography**
   - Crossed asymmetry: pre-chiasmatic
   - Uncrossed asymmetry: post-chiasmatic (Cortex, optic radiation)

4) **“W” Shape**
   - Pre-chiasmatic
   - Technical, normal variation
Case 1

<table>
<thead>
<tr>
<th>PRVEP</th>
<th>Flash VEP</th>
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<tbody>
<tr>
<td>Trial</td>
<td>N75 (ms)</td>
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<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Trial7 - R</td>
<td>69.9</td>
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<tr>
<td>Trial8 - L</td>
<td>85.9</td>
</tr>
<tr>
<td>L-R Norm</td>
<td>&lt;17</td>
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Male, 39 years old, with sudden onset of decreased visual acuity in LE. Neurosífilis and HIV. MRI showed no brain lesions, nor optic nerve injury. 
Ophthalmologic evaluation: Panuveitis and inflammatory disc edema. Localization: Ocular
Notice abnormalities in PRVEP but not in Flash VEPs. Given the deficits of the LE vision, PRVEP were abnormal.
### PRVEP

<table>
<thead>
<tr>
<th>Trial</th>
<th>N75 (ms)</th>
<th>P100 (ms)</th>
<th>N145 (ms)</th>
<th>N75-P100 (µV)</th>
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<tr>
<td>Norm</td>
<td>&lt;117</td>
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<tr>
<td>Trial4 - L</td>
<td>67.2</td>
<td>92.6</td>
<td>131.3</td>
<td>9.98</td>
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<tr>
<td>Trial8 - R</td>
<td>75.4</td>
<td>110.9</td>
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<td>L-R Norm</td>
<td>&lt;8</td>
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<tr>
<td>L-R</td>
<td>8.2</td>
<td>18.3</td>
<td>16.4</td>
<td>6.60</td>
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### Case 2

Female, 30 years old, with 8 days history of right ocular pain, decreased visual acuity, phosphenes, incapacity to distinguish colors. No previous medical history.

MRI shows enhancement of right optic nerve at the intraorbital, intracanal, and intracranial segments.

Localization: **Pre-chiasmatic**
Case 3

Female, 60 years old, bilateral restricted visual fields, predominantly on the RE. History of benign sellar tumor removed the previous year. Post-operative MRI shows intrasellar fluid collection, with chiasmatic luxation, predominantly towards the left side. Localization: **Chiasmatic**
Lesion on the left optical tract, RE stimulation
Lesion on the left optical tract, LE stimulation

Left cortex y deafferented, therefore there is no activity that projects to the RO Uncrossed abnormality
Clinical Applications

Prechiasmatic Lesions

1) **Multiple Sclerosis**: Optic Neuritis is the main reference to perform PRVEP. In the acute phase, when vision is lost, the PRVEP are lost, and as vision returns, amplitude of the P100 recover, but not latencies. In fact, even with normal vision, patients may present for long periods of time, normal P100 morphology with prolonged latencies (like biological marker of ON) due to the demyelination process.

2) **Tumors**: Optic nerve tumors, affect morphology more importantly than latencies, since not all fibers of the ON are affected, and the remaining fibers can conduct the visual information. Larger tumors may block completely the visual pathway.

3) **Neuropathies**: can cause amplitude changes as well as latency prolongation, depending on the type of neuropathy: demyelinating Vs: axonal.

4) **Metabolic Disorders**: Leukodystrophies, Krabbe Disease and several other, may cause prechiasmatic or postchiasmatic lesions. Depending on the clinical stage, abnormalities will be different.

5) **Conversive blindness**: Caution should be taken with these patients, since they will not cooperate to fixate the checkerboard and cause low amplitude and increased latency. So, flash VEP can be used instead.
Clinical Applications

Chiasmatic Lesions (crossed abnormalities)

1) Lesions on the Sella Turcica. Craniopharyngiomas, Pituitary Tumors: Compression of the optic chiasma produce distortion of the VEPs, mainly amplitude and less effects on latency. Monocular hemifield and full field stimulation may help to determine the localization, by observing “crossed asymmetry”.
Clinical Applications

Postchiasmatic Lesions (uncrossed asymmetries)

1) **Lesions on the posterior visual pathway (LGN, Cortex).** Ischemic, demyelinating lesions, tumors, hemorrhagic, produce distortion of the VEPs, mainly amplitude and less effects on latency. Uncrossed asymmetry of the parasagittal P100 with monocular stimulation is typical. Binocular hemifield stimulation should be done to corroborate localization.

2) **Neurodegenerative Disorders:** Dementias (Alzheimer, Parkinson), metabolic disorders (leukodystrophies) may cause bilateral lesions. Most of these lesions, cause bilateral changes in amplitude, also latency prolongation may be seen. Specially because these patients do not cooperate in the test (lack of fixation on the screen).
Clinical Applications

Ophthalmologic Disorders

1) Refractive errors
2) Glaucoma
3) Amblyopia
4) Disorders of the anterior chamber
5) Various types of retinal pathologies

VEPs are not routinely applied to these pathologies, but when used, most of the times, changes in amplitude and latencies can be seen, depending on the seriousness of the lesions.
Conclusions

VEPs may provide important diagnostic information regarding the functional integrity of the visual system. Increments in latency with relatively preserved waveform morphology is a signal of a demyelinating pathology. Distortions of morphology with no changes in latency may traduce compression.

VEPs help to confirm the presence of visual pathology or to detect subclinical asymptomatic involvement of the visual pathway.

In healthy subjects, PRVEP latencies are influenced by stimulus-related variables such as luminance, spatial frequency, contrast. Other factors like fixation on the screen are of paramount importance.

Pattern reversal is the favored stimulus for most clinical purposes.

Flash VEPs are useful when poor optics, lack of cooperation or poor vision, malingering and patients with nystagmus.

Utilization of central and parasagittal electrodes are useful to localize lesions of the visual pathway.
Conclusions

Normal VEP practically exclude abnormalities of the optic nerve

VEP is superior in cases of optic nerve and anterior chiasmatic lesions than MR, but the later is clearly superior in retrochiasmatic diseases

VEP remain abnormal over long periods in patients with Optic Neuritis due to MS, despite recovery of visual acuity

Objective and reproducible test for optic nerve function

Inexpensive as compared with to MRI

Under certain circumstances, may be helpful to positively establish optic nerve function in patients with subjective complaint of visual loss