Visual Evoked Potential (VEP) Delays in Central Serous Choroidopathy

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The authors examined a series of ten consecutive patients with unilateral, idiopathic central serous choroidopathy. Visual acuities ranged from 20/20 to 20/70 during the active stage. VEPs were recorded to square sizes of 14, 28, and 56 min of arc. Overall, 90% of the patients had statistically significant VEP delays from the affected eye, while only 30% had statistically significant reductions in amplitude during the active stage. Six of the ten patients were reevaluated after the condition fully resolved. In all six, the VEP latency returned to normal. Although the mechanism of these VEP delays is not clear, their presence has been well documented. Therefore, a VEP delay in isolation of other tests should not be used in the differential diagnosis of macular vs optic nerve disease. One should specifically rule out macular disease in any patient with a delayed VEP before presuming the presence of a visual pathway dysfunction. Invest Ophthalmol Vis Sci 27:214–221, 1986

Delays in the visual evoked potential (VEP) are widely used to support a diagnosis of optic neuropathy and demyelinating disease.1 VEP delays have also been reported in other diseases, such as spinocerebellar degeneration,2 Friedreich's ataxia,3 Parkinson's disease,4-6 vitamin B12 deficiency,7-9 diabetes without retinopathy,10 use of select drugs,11,12 as well as in conditions which may result in degradation of retinal images, such as cataracts and pupillary miosis. Nevertheless, a delayed VEP is still considered to be the hallmark of optic nerve demyelination.

There is a relative paucity of data, however, documenting the presence of VEP delays in macular disease. Some investigators have reported VEP phase shifts in macular disease,13 and Lennerstrand14 has reported abnormal VEP latencies in a majority of patients having macular lesions. In addition, Bodis-Wollner and Feldman15 reported delayed transient VEPs and attenuated steady state VEPs in two patients with old, inactive perimacular lesions.

We recently reported significant monocular VEP delays in 45% of patients having either acquired unilateral or asymmetric bilateral maculopathy.16,17 Of the 20 patients studied, a delay of 26 msec was documented in the eye of a patient having unilateral idiopathic central serous choroidopathy with normal visual acuity. Because this patient demonstrated the largest VEP delay of all our maculopathy patients and because VEP delays in central serous choroidopathy had never previously been reported, we decided to limit this current study to central serous choroidopathy patients. This disease entity was an ideal one to study because (a) it is often a reversible, limited condition which resolves with or without treatment; (b) there is usually a normal control eye; (c) the typical time course of its resolution is favorable for detailed investigation.

There have recently been two additional reports18,19 following ours16 in which VEP delays have also been documented in patients with central serous choroidopathy. In this current study, we performed VEPs on a series of ten patients who were diagnosed as having unilateral idiopathic central serous choroidopathy. We followed seven of these patients until the condition either fully resolved (six patients) or partially resolved (one patient). Unlike previous reports, we will demonstrate that as the condition resolves, the VEP returns to normal and becomes nearly superimposable with the VEP from the unaffected eye.

Materials and Methods

We evaluated ten consecutive patients (ranging in age from 27 to 49 yr, with a mean age of 38.8 yr) diagnosed as having active central serous choroidopathy in one eye (Table 1). All patients had the typical ophthalmoscopic and fluorescein angiographic finding of serous detachment of the neurosensory retina in the macula. Each patient had normal pupillary responses and normal-looking optic discs. The ocular examination was otherwise normal except for serous detachments of the retinal pigment epithelium (RPE) outside

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the macula in the fellow eye in two patients (patient 6, patient 8) and one patient with bilateral kera-toconus (patient 4). Visual acuities ranged from 20/20 to 20/70 in the affected eye during the active phase. Informed consent was obtained from each patient prior to undertaking the study.

Pattern-reversal VEPs were recorded from each eye separately, using an averager ( Nicolet CA–1000) and visual stimulator ( Nicolet 1005, Madison, WI). A gold cup electrode ( Grass; Quincy, MA), attached to the scalp 2 cm above the inion, was used to record the VEP. Two ear clip electrodes were used, one for the reference and the other for the common ground. Electrode impedance was maintained below 6000 Kohms. An artifact rejection was utilized to reject any signal greater than about 50 µV which might be created by blinks or large eye movements. Pattern elements consisted of squares of 14, 28, and 56 min of arc presented in a checkerboard pattern. The pattern elements were measured by their edge and not diagonally. The pattern was reversed at 7.5 reversals/sec. The stimulus distance was 1 meter. The overall field size at 1 m was 12° vertical by 15° horizontal. Mean luminance was maintained at 25 cd/m² and contrast (L max – L min)/(L max + L min) at 76%. The patients were optically corrected for the stimulus distance and mydriatics and cycloplegics were not utilized. The analysis time was set at 200 msec, and between 100 and 200 responses were averaged for each trial.

VEP amplitudes on all patients were determined by measuring the difference between the major positive and major negative peaks. Peak times (to be referred to as “latency”) were taken from the stimulus trigger to the highest positive peak. We have elected not to use the standard nomenclature of P100, P135 etc because the standard reversal rate of 1 HZ (2 reversals/sec) was not utilized (see above). In addition to measuring monocular latency and amplitude, interocular latency and amplitude differences were calculated. The absolute value of these interocular differences were compared to a control group consisting of 16 normals, evaluated as part of a previous study performed by these authors17 (Table 2). If an interocular difference (either amplitude or latency) of a patient was greater than 2.5 standard deviations from the mean interocular difference of the control group, we considered the difference to be statistically significant.

**Results**

The results of the VEPs in the active stage and resolved stage in these ten cases are listed in Table 1. Three patients were lost to follow-up. The mean latency in the normal unaffected eyes was 116 ± 5.1 msec to 14-min squares, 109.8 ± 6.7 msec to 28-min squares, and 108.8 ± 6.7 msec to 56-min squares. The mean latency of the central serous eyes (during the active phase) was 136.8 ± 11.8 msec to 14-min squares, 126.5 ± 15.4 msec to 28-min squares, and 120.9 ± 10.5 msec to 56-min squares (Table 3).

The central serous eye compared to the normal eye demonstrated a mean VEP delay of 21 ± 10.3 msec to 14-min squares, 16.7 ± 9.2 msec to 28-min squares, and 10.6 ± 6.0 msec to 56-min squares (Table 4).

Individually, 7 of the 8 patients (88%) giving recordable responses to 14-min squares demonstrated statistically significant interocular VEP delays. All 10 patients gave recordable responses to 28-min squares, and 7 of these (70%) demonstrated statistically significant interocular VEP delays. Nine patients gave recordable responses to 56-min squares, and of these 9, 5 (56%) demonstrated statistically significant interocular VEP delays. When considering all 3 square sizes, 9 out of 10 patients (90%) had significant interocular delays in the affected eye.

When analyzing the data for effects on amplitude, we found that only 13% of the patients (1 out of 8) demonstrated statistically significant interocular reductions in amplitude to 14-min squares, 20% (2 out of 10) to 28-min squares, and 22% (2 out of 9) to 56-min squares. Overall, 30% of patients demonstrated a significant decrease in amplitude when considering all three square sizes.

**Case Reports**

Three exemplary cases are presented here with findings confirming the diagnosis of idiopathic central serous choroidopathy and VEPs performed during the active phase and repeated after the condition resolved. Case 1 was treated with laser 2 wk after the diagnosis was established. Case 2 was followed for 6 months without spontaneous resolution of the fluid and then treated with laser. Case 3 fully resolved spontaneously within 7 months.

*Case 1.* Patient 6, a 39-yr-old white policeman, presented with a complaint of a “dark spot” in his vision in the left eye for the past 6 months. Best corrected visual acuities were 20/20 in the right eye and 20/30 in the left eye. Ophthalmoscopy revealed a large area of fluid in the macula of the left eye and RPE changes in the macula of the right eye. On Amsler grid, the neurosensory retina infero-temporal to the fovea (Fig. 1). VEPs recorded from the left eye demonstrated significant interocular delays to all 3 square sizes with a 43 msec delay to 14-min squares (the largest delay recorded from any patient in our study), Figure 2A, a 12 msec delay to 28-min squares, and a 16-msec delay to 56-min squares. The interocular amplitude differences were not statistically significant. Because the condition had failed to resolve spontaneously, the patient was eager to undergo laser photocoagulation, which was performed by a local ophthalmologist. Three weeks after treatment, the patient returned to us. The initial symptoms had
The condition had failed to resolve spontaneously, the patient was eager to undergo laser photocoagulation, which was performed by a local ophthalmologist. Three weeks after treatment, the patient returned to us. The initial symptoms had disappeared, but the patient was now aware of a scotoma. Three weeks after treatment, the patient's subjective symptoms disappeared and visual acuity improved in the affected eye to 20/20. Ophthalmoscopy revealed some RPE defects and 35 sec in the left eye. VEPs recorded from the left eye achieved a visual acuity of 20/50 and 24 sec in the left eye. Since the fluid failed to resorb and leakage was still evident, the patient decided to have laser photocoagulation performed. Three weeks after treatment, the patient's subjective symptoms disappeared and visual acuity improved in the affected eye to 20/20. Ophthalmoscopy revealed some RPE defects nasal to the fovea, but fluid was no longer evident. On Amsler grid viewing, metamorphopsia was not present, but a 6° scotoma was now normal, did not exhibit any delays compared with the right eye and were practically superimposable (Fig. 2B).

Case 2. Patient 5, a 38-yr-old white postal worker presented with complaints of a "blurry spot" in the center of his field of vision in the left eye of approximately 1 month's duration. Entering visual acuities were 20/20 in the right eye and 20/25 in the left eye. Ophthalmoscopy of the left eye revealed edema residues in the left macula with paramacular edema. The right eye was unremarkable. On viewing the Amsler grid, the patient reported a 7° circular area of metamorphopsia around the fixation point in the left eye. Viewing with the right eye did not reveal any abnormalities. Macular dazzle recovery time was 1 min in the right eye to read 20/25 and 25 min in the left eye to read 20/40. Fluorescein angiography revealed a serous detachment of the neurosensory retina supero-nasal to the fovea in the left eye (Fig. 3). VEPs were recorded and interocular delays were evident to all three square sizes (Fig. 4A), with an 18-msec delay from the affected eye to 14-min squares, a 19-msec delay to 28-min squares, and a 20-msec delay to 56-min squares. The interocular amplitude differences were not statistically significant. The patient was followed monthly for the next 5 months during which time there was no change in acuity, symptoms, ophthalmoscopic appearance, or VEP latency. After the sixth month of follow-up, fluorescein angiography was repeated. Since the fluid failed to resorb and leakage was still evident, the patient was followed monthly for the next 5 months during which time there was no change in acuity, symptoms, ophthalmoscopic appearance, or VEP latency. After the sixth month of follow-up, fluorescein angiography was repeated. Since the fluid failed to resorb and leakage was still evident, the patient decided to have laser photocoagulation performed. Three weeks after treatment, the patient's subjective symptoms disappeared and visual acuity improved in the affected eye to 20/20. Ophthalmoscopy revealed some RPE defects nasal to the fovea, but fluid was no longer evident. On Amsler grid, the patient did not report any metamorphopsia in either eye. Photostress recovery times were 15 sec in the right eye and 35 sec in the left eye. VEPs recorded from the left eye were now normal, did not exhibit any delays compared with the right eye and were practically superimposable (Figure 4B).

Case 3. Patient 1, a 40-yr-old white male, presented with complaints of seeing a film over the right eye and a "halo" in the center of his vision. Visual acuities were 20/20 through the left eye. Examination of the right eye through a Goldmann 3-mirror lens revealed edema of the central 7° of the retina. The central retina of the left eye was within normal limits. Drusenlike changes were evident throughout the posterior poles of both eyes. Testing with the Amsler grid revealed an approximately 7° central, round relative scotoma when viewed through the right eye. No visual field abnormalities were evident when viewing the Amsler grid through the left eye. Results of macular dazzle revealed recovery times of 300 sec in the right eye to achieve a visual acuity of 20/50 and 24 sec in the left eye to achieve 20/20. Fluorescein angiography revealed a serous detachment of the neurosensory retina supero-nasal to the macula in the right eye (Fig. 5). VEPs were recorded to
Table 2. Mean values for VEP Latency, amplitude and latency, amplitude difference between eyes of 16 normal controls (32 normal eyes)

<table>
<thead>
<tr>
<th>Square size</th>
<th>Mean latency (msec)</th>
<th>Mean amplitude (µV)</th>
<th>Mean difference in latency (msec)</th>
<th>Mean difference in amplitude (µV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 minute</td>
<td>119.2 ± 8.4</td>
<td>9.8 ± 3.9</td>
<td>2.9 ± 3.1</td>
<td>1.9 ± 2.0</td>
</tr>
<tr>
<td>28 minute</td>
<td>113.4 ± 7.6</td>
<td>9.8 ± 3.7</td>
<td>3.7 ± 2.6</td>
<td>1.6 ± 1.1</td>
</tr>
<tr>
<td>56 minute</td>
<td>110.6 ± 7.2</td>
<td>8.9 ± 3.2</td>
<td>3.8 ± 4.3</td>
<td>2.1 ± 1.4</td>
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</tbody>
</table>

Table 3. Mean values for VEP latency and amplitude for the unaffected eye and for the affected eye of ten central serous choroidopathy patients

<table>
<thead>
<tr>
<th>Square size</th>
<th>Unaffected eyes</th>
<th>Affected eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean latency (msec)</td>
<td>Mean amplitude (µV)</td>
</tr>
<tr>
<td>14 min</td>
<td>116.0 ± 5.1</td>
<td>8.7 ± 4.9</td>
</tr>
<tr>
<td>28 min</td>
<td>109.8 ± 6.7</td>
<td>7.8 ± 3.3</td>
</tr>
<tr>
<td>56 min</td>
<td>108.8 ± 6.7</td>
<td>8.5 ± 3.0</td>
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Table 4. Mean values for interocular latency and amplitude differences in central serous choroidopathy patients

<table>
<thead>
<tr>
<th>Square size</th>
<th>Mean latency difference (msec)</th>
<th>Mean amplitude difference (μV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 min</td>
<td>21.0 ± 10.3</td>
<td>3.2 ± 3.6</td>
</tr>
<tr>
<td>28 min</td>
<td>16.7 ± 9.2</td>
<td>3.0 ± 3.2</td>
</tr>
<tr>
<td>56 min</td>
<td>10.6 ± 6.0</td>
<td>2.9 ± 3.9</td>
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in the right eye and 10 sec in the left eye. No abnormalities were reported when viewing the Amsler grid. VEPs revealed negligible differences in the peak times of the responses from the right and left eyes (Fig. 6B).

Discussion

Idiopathic central serous choroidopathy, a clinical entity primarily seen in young males, is characterized by a flat, serous detachment of the sensory retina of the posterior pole and is usually a benign, self-limiting condition which resolves spontaneously. Generally, treatment with laser photocoagulation is employed if resolution does not occur spontaneously within 4-6 months. To our knowledge, when we first reported significant interocular VEP delays in a patient having unilateral, idiopathic central serous choroidopathy as part of a larger study on maculopathy patients, there had been no previous reports of VEP delays occurring in this condition. More recently, however, Papakostopoulos, et al\(^\text{18}\) have reported mean interocular VEP delays of 7.3 msec in 6 patients having unilateral, central serous choroidopathy and Han, et al\(^\text{19}\) presented evidence of VEP delays in 18 patients having this condition. Unlike these two reports, in the present study we demonstrated that as the unilateral condition resolves, the VEP returns to normal and becomes nearly superimposable with the VEP from the unaffected eye.

The mechanism(s) responsible for VEP delays in central serous choroidopathy is unknown. The fluid may cause receptor tilt resulting in an abnormal Stiles-Crawford Effect which decreases the efficiency of light energy. Figure 7 demonstrates that a series of neutral density filters progressively delays the VEP from a normal eye while causing only minimal reduction in am-

![Image](https://iovs.arvojournals.org/pdfsaccess.ashx?url=/data/journals/iovs/933358/)
Fluorescein angiography of the left eye revealed a large area of leakage supero-nasal to the fovea. A second area, temporal to the fovea, did not increase in size from the early to the late phase; left, early phase, right, late phase.

Fig. 3. Fluorescein angiography revealed a small area of leakage supero-nasal to the macula in the right eye; left, early phase, right, late phase.

Fluorescein angiography of the left eye revealed a large area of leakage supero-nasal to the fovea. A second area, temporal to the fovea, did not increase in size from the early to the late phase; left, early phase, right, late phase.

Fig. 4. Left, VEPs recorded during the active phase; 18-msec interocular delay, O.S., demonstrated. Right, VEPs recorded once condition fully resolved; no interocular delay evident from the left eye; responses are superimposable.

A.

B.

6/13/83
VA: OD-20/20-3
OS-20/30-2

VEPs recorded during the active phase; 18-msec interocular delay, O.S., demonstrated. Right, VEPs recorded once condition fully resolved; no interocular delay evident from the left eye; responses are superimposable.

Another possible mechanism is that the fluid impairs the integrity of the neuronal membranes, thus interfering with dynamics of neurotransmitter action involved in the intraretinal feedback loop modulating adaptational processes. The best neurotransmitter candidate for such modulatory activity is dopamine, which has recently been found in the human retina. VEP delays in dopaminergic deficiency due to Parkinson's disease (PD) have been demonstrated by Bodis-Wollner and Yahr, who proposed a retinal origin of the delays.
More recently, Kupersmith et al.\(^6\) in addition to finding VEP delays in a group of PD patients, recorded oscillatory potential electroretinograms in the same group. These potentials are believed to reflect activity in the inner nuclear layer and are probably mediated by the amacrine cells.\(^{25}\) or the interplexiform cells.\(^{26}\) Since both cell types contain dopamine\(^{27,28}\) and since the application of dopamine to the retina in vitro alters the oscillatory potential,\(^{29}\) one might expect abnormal oscillatory potentials in PD. However, Kupersmith et al.\(^6\) report normal oscillatory potentials in the same group of patients with PD who demonstrated VEP delays. Although these results do not support the contention that a dopamine deficiency exists at the retinal level in PD, they cannot preclude the retina as a possible site of dysfunction in PD.\(^6\)

One may argue that since the VEP is normally a macular-dominated response, any macular lesion, such as CSR, may uncover a paramacular potential which normally has a greater latency.\(^{30}\) In normal patients, this paramacular potential is often hidden in the earlier and larger macular potential. However, upon careful inspection of the VEP waveforms from the nine CSR patients with delays reported in this study, one observes that the positive and negative waves appear to be delayed in the affected eye when compared with the unaffected eye, rather than the absence or reduction of just the major positive peak.

Wildberger\(^{31}\) has shown that stimulation of the lower half of the retina results in VEPs which are approximately 20 msec later than those resulting from stimulation of the upper half of the retina. This suggests that a lesion affecting only the upper half of the macula may result in a delayed VEP. In the nine patients with CSR with delays reported in this study, three had lesions primarily inferior to the fovea, three had lesions primarily superior to the fovea, and three had relatively central lesions. No correlation exists between the location of the detachment and the latency delay.

Although the explanation of VEP delays in central serous choroidopathy will be the subject of ongoing study, the presence of these delays has been well demonstrated in this preliminary study and in other reports as well. A delayed VEP to squares of various spatial frequencies can therefore no longer be used in the differential diagnosis of CSR vs demyelinating optic nerve dysfunction. If VEPs to squares are delayed, macular disease, especially central serous choroidopathy, must be ruled out before diagnosing a visual pathway dysfunction. This point is not trivial since Kraushar\(^{32}\) has reported three patients diagnosed by ophthalmologists as having multiple sclerosis who actually had recurrences of central serous choroidopathy, which was proven angiographically. Since both central serous choroidopathy and multiple sclerosis produce episodes of monocular visual loss in young adults, misdiagnosis is possible especially in those cases with only minimal fluid accumulation. In such questionable cases, the clinician should simply rely upon the results of the swinging flashlight test, macular dazzle, color vision, and fluorescein angiography, but certainly not the VEP.

**Fig. 7.** When less light reaches the photoreceptors as a result of the interposition of a series of neutral density filters (NDF), the VEP becomes progressively delayed.
Although we have demonstrated that VEPs to squares are not useful alone for differential diagnosis, VEPs to gratings might be since VEP delays to gratings of some orientations but not to others have been reported in multiple sclerosis\(^3\) but not in macular disease. It remains to be demonstrated whether such VEP orientation asymmetries will permit the differential diagnosis of macular vs optic nerve dysfunction to be made with any certainty.

Finally, the general guideline sometimes espoused by clinicians that VEPs are delayed in optic nerve disease but reduced in amplitude in retinal disease should be abandoned. Not only do delays as great as 43 msec occur in retinal disease (Case 1), but many cases of non-demyelinating optic neuropathies have no (or only slight) VEP delays.\(^{34,35}\) Reductions in amplitude, both in retinal disease and optic neuropathies, grossly correlate with the visual acuity reduction.\(^3\)

**Key words:** central serous chorioidopathy, visual evoked potential delays, macular disease, optic nerve disease

**References**