The Focal Electroretinogram in the Clinical Assessment of Macular Disease

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Abstract: Focal electroretinograms (ERGs) were obtained from the fovea in 142 eyes with a variety of macular diseases and 50 age-matched eyes with acuity loss in which macular disease was ruled out. Across all eyes, the accuracy rate of discriminating macular disease from other causes of acuity loss was 87%. Among all eyes with macular disease, the sensitivity rate of the focal ERG to the presence of macular disease was 85%. Log focal ERG amplitude was significantly correlated with log Snellen acuity, except in those eyes with macular holes. The sensitivity rate increased to 94% when eyes with 20/40 or greater acuity and eyes with macular holes were excluded. Ophthalmology 96:109–114, 1989

Previous studies have shown that the focal electroretinogram (ERG) can provide an objective measure of central retinal function.[1–14] Focal ERGs are typically reduced in amplitude in retinal diseases such as retinitis pigmentosa,[3,8,10,11] hereditary macular degeneration,[3,11–13] central serous retinopathy,[8] and age-related macular degeneration.[3–5] Normal focal ERGs have been reported in amblyopia[15,16] and optic neuropathy.[17] Along with helping to localize the site of abnormality, focal ERGs are useful for following patients with progressive retinal disease.

The possible usefulness of the focal ERG in a clinical environment has not been systematically evaluated. It is necessary to know the accuracy of the focal ERG for discriminating visual loss because of macular disease from loss due to other causes before this technique can be used to determine macular integrity in, for example, eyes with cataracts or other media opacities. In the current study, focal ERGs were measured in 142 eyes with diagnosed maculopathy and in 50 eyes with reduced acuity due to causes other than maculopathy. One goal of the study is to reevaluate the correlation reported previously[4,11,12] between focal ERG amplitude and best-corrected Snellen acuity by testing a large group of patients with diverse forms of maculopathy. A second goal was to evaluate the diagnostic value of the focal ERG by assessing the sensitivity, specificity, and accuracy rates of the focal ERG in detecting macular disease.

PATIENTS AND METHODS

PATIENTS

Focal ERGs were obtained from 142 eyes of 108 patients with clear media and a variety of macular diseases. In patients with bilaterally symmetric conditions such as juvenile macular degeneration, one eye was randomly selected for the analysis. Responses from both eyes were included for patients with diseases, such as age-related macular degeneration, that typically affect each eye differently. The best-corrected Snellen visual acuity was obtained for each eye. The number of eyes in each diagnostic category is shown in Table 1. The relatively large number in certain diagnostic categories reflects research interests

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Table 1. Diagnoses of Eyes with Macular Disease

Diagnoses	No. of Eyes
Age-related macular degeneration	26
Central areolar choroidal sclerosis	2
Cystoid macular edema	3
Cone dystrophy	10
Central retinal vein occlusion	1
Central serous retinopathy	1
Diabetic retinopathy	6
Hereditary macular degeneration	33
X-linked juvenile retinoschisis	1
Macular hole	43
Macular traction	1
Presumed ocular histoplasmosis	1
Retinal detachment	1
Retinal telangiectasia	2
Retinitis pigmentosa	11
Total	142

Table 2. Diagnoses of Eyes without Macular Disease

Diagnoses	No. of Eyes
Amblyopia	2
Cataract	23
Functional vision loss in children	9
Optic neuropathy	7
Unknown	9
Total	50

of the authors. Focal ERGs were also obtained from 50 eyes of patients with reduced acuity due to causes other than maculopathy. The best-corrected Snellen acuity was obtained in each eye. The number of eyes in each diagnostic category is shown in Table 2. Cataracts in some eyes reduced visual acuity as low as 20/200 but did not preclude an adequate view of the fundus for focal electroretinography. Absence of macular disease was confirmed after cataract surgery when all eyes achieved greater than 20/25 visual acuity. The mean age of patients without maculopathy (41.3 years) was not significantly different ($t = 1.75$) from the mean age of patients with maculopathy (48.6 years).

METHODS

Pupils were dilated before testing. Using a Burian-Allen bipolar contact lens electrode and a hand-held stimulator ophthalmoscope, focal ERGs were measured by placing a stimulus on the macula under direct observation.[9] Recording was controlled by a foot pedal so that responses were obtained only when stimulating the fovea. A 3° achromatic, flickering test spot (42 Hz) was centered within a 10° achromatic, steady annular surround. Possible stray light responses were eliminated by having a higher retinal illuminance in the annulus (5.3 log trolands) than in the stimulus (4.8 log trolands).

The responses were amplified both differentially (gain = 50,000) and selectively (gain = 20) at the stimulus frequency (Q = 15). Averaged responses (n = 200) were obtained on a Digital PDP 11/23 computer (Maynard, MA) with a data acquisition program containing an artifact rejects subroutine. At least two averaged responses were obtained from each fovea. Mean peak-to-peak amplitude and mean implicit time (time from stimulus to positive peak) were determined from the computer-averaged responses. Mean (±1 standard deviation) foveal amplitude in 100 normal eyes tested with the same procedure was 0.31 ± 0.08 μV, with a mean (±1 standard deviation) implicit time of 33.6 ± 1.8 msec.[4] Focal amplitudes of less than 0.18 μV and implicit times greater than 36.6 msecond were considered abnormal ($P < 0.05$) in the current study. The average noise level with the stimulus occluded was 0.06 μV.[4]

RESULTS

In Figure 1, representative focal ERGs from patients with reduced acuity due to maculopathy (left column) or causes other than maculopathy (right column) are shown. Two repetitions of each average are shown to demonstrate repeatability. Vertical spikes represent stimulus onset. In general, amplitude from the fovea decreased with decreasing Snellen acuity in eyes with maculopathy, but was unrelated to acuity in eyes without maculopathy. As shown in Figure 2, a significant inverse relationship ($r = -0.85$; $P < 0.001$) was found between mean log focal ERG amplitude and log Snellen acuity for the 142 eyes with macular diseases (closed circles). Because mean log focal ERG amplitude was not significantly correlated with log Snellen acuity in the 43 eyes with macular holes ($r = 0.44$), the relationship is also shown separately in Figure 1 for the 99 eyes with maculopathy excluding those with macular holes (open circles). Excluding eyes with full-thickness macular holes increased the correlation between mean log focal ERG amplitude and log Snellen acuity ($r = 0.94$; $P < 0.001$). It is also evident from the size of the 95% confidence intervals for the means in Figure 1 that precise relationships between Snellen acuity and focal amplitude do not exist for individual eyes.

FOCAL ELECTRORETINOGRAM VERSUS MACULOPATHY

For the following data, a simple and practical analysis divides the eyes into those with and without macular disease and the measured focal ERG as normal or abnormal. Separate analyses were conducted for amplitude (abnormal, <0.18 μV), implicit time (abnormal, >36.6 msecoonds) and combined parameters (abnormal amplitude and/or implicit time). The results are presented in 2 × 2 contingency tables, with definitions in Table 3.

In all eyes. Table 4 displays the results in all 192 eyes. Table 4, top, shows that 110 eyes with maculopathy had reduced focal ERG amplitudes (true-positives), whereas 32 eyes with maculopathy had normal focal ERG amplitudes (false-negatives). The sensitivity rate for detecting

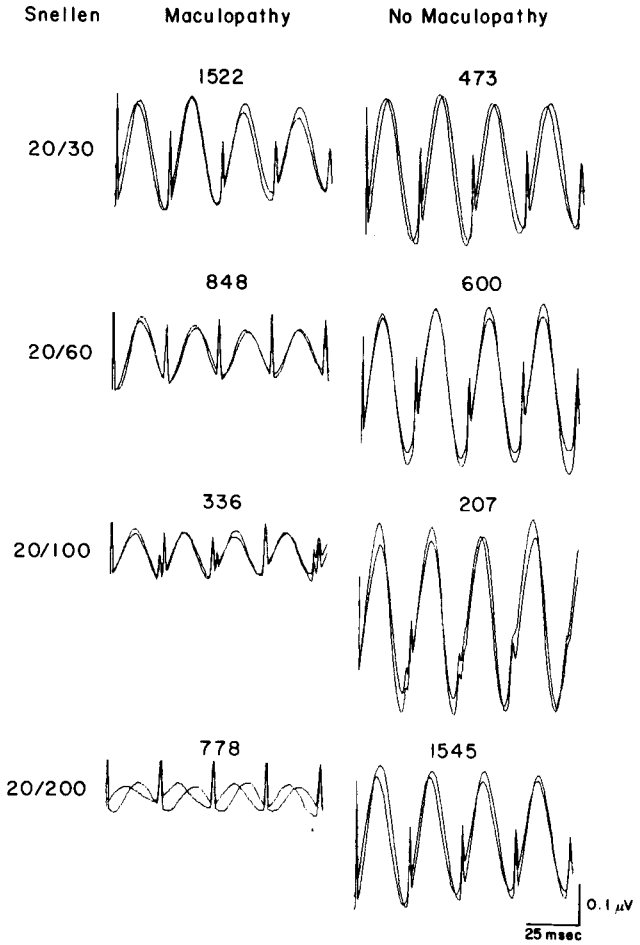

Fig 1. Focal ERGs from representative eyes of patients with reduced acuity due to maculopathy or causes other than maculopathy. Two repetitions of each foveal response are shown to demonstrate repeatability. Vertical spikes are superimposed artifacts to indicate stimulus onset. In eyes with maculopathy, patient 1522 had cystoid macular edema, patient 848 had hereditary macular degeneration: patient 336 had age-related macular degeneration; and patient 778 had diabetic retinopathy. In eyes without maculopathy, patient 473 had strabismic amblyopia; patient 600 had functional acuity loss; patient 207 had optic neuropathy; and patient 1545 had nuclear cataract.

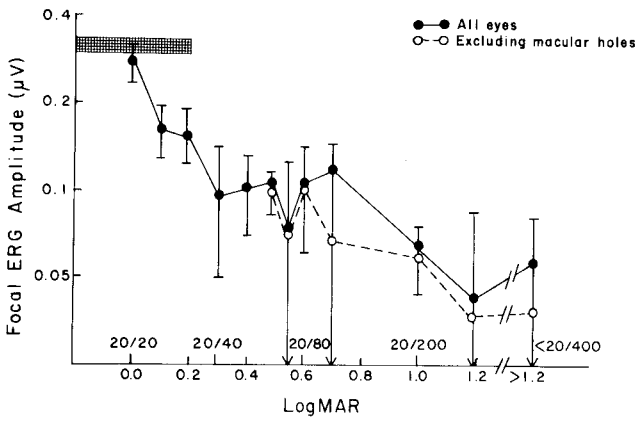

Fig 2. The relationship between mean log focal ERG amplitude and log Snellen acuity (logMAR) in eyes with maculopathy is illustrated. Closed circles represent all 142 eyes. Open circles represent all eyes with maculopathy excluding eyes with full-thickness macular holes. Vertical lines represent the 95% confidence interval for each mean. The 95% confidence interval for mean normal is shown as a hatched rectangle.

Table 3. Definitions*

	Maculopathy	No Maculopathy
Abnormal test	A	B
Normal test	C	D

* Sensitivity = A/A + C; specificity = D/B + D; accuracy = A + D/A + B + C + D.

maculopathy on the basis of amplitude was, therefore, 77%. Of the eyes without maculopathy only 2 of 50 had reduced focal ERG amplitudes, a specificity rate of 96%. The overall accuracy rate of focal ERG amplitude for detecting maculopathy was 82%. Table 4, center, shows that focal ERG implicit time was somewhat less effective in identifying eyes with maculopathy. However, when both amplitude and implicit time were used as criteria (Table 4, bottom), the overall accuracy rate of the focal ERG for discriminating maculopathy from other causes of visual loss rose to 87%.

Eyes with macular holes only. As noted previously, focal ERG amplitude was poorly correlated with Snellen acuity in patients with macular holes. However, focal ERG amplitude was found to have a sensitivity rate of 79% for detecting maculopathy in eyes with macular holes (Table 5, top), very near that of the group including all eyes with maculopathy. Implicit time alone (Table 5, center) was not particularly helpful in detecting macular holes (sensitivity rate, 46%) and using the combined criteria of amplitude and/or implicit time had little effect on the overall accuracy (Table 5, bottom).

To further evaluate the value of the focal ERG as a diagnostic test, eyes were divided into two groups according to the best-corrected Snellen acuity. Eyes with 20/40 or better visual acuity were considered to have good vision, whereas eyes with visual acuity of less than 20/40 were considered to have poor vision. This rather arbitrary division was selected because 20/40 or better visual acuity is generally considered an acceptable result after cataract surgery and allows the patient to read without difficulty. Of 32 eyes with maculopathy retaining good vision, 21 had either reduced focal ERG amplitude or delayed implicit time for a sensitivity of 66%. The remaining 110 eyes with maculopathy had less than 20/40 Snellen acuity.

Eyes with reduced visual acuity (<20/40). Table 6 displays the results in eyes with less than 20/40 visual acuity. Ninety-four eyes had reduced focal ERG amplitude, a positive test (Table 6, top). Sixteen eyes had normal focal ERGs, a negative test. The sensitivity of focal ERG amplitude was 86% in detecting eyes with maculopathy in eyes which had reduced vision. In the eyes with reduced

Table 4. Focal Electroretinogram versus Maculopathy in All Eyes

	No. of Eyes		Sensitivity (%)	Specificity (%)	Accuracy (%)	Chi-square	*P*
	Maculopathy	No Maculopathy					
Amplitude							
Reduced focal ERG	110	2					
Normal focal ERG	32	48					
			77	96	82	79.1	≤0.001
Implicit time							
Delayed focal ERG	66	2					
Normal focal ERG	76	48					
			46	96	59	27.3	≤0.001
Combined amplitude/implicit time							
Reduced/delayed focal ERG	121	4					
Normal focal ERG	21	46					
			85	92	87	93.7	≤0.001

ERG = electroretinogram.

Table 5. Focal Electroretinogram versus Maculopathy in Eyes with Macular Holes Only

	No. of Eyes		Sensitivity (%)	Specificity (%)	Accuracy (%)	Chi-square	*P*
	Maculopathy	No Maculopathy					
Amplitude							
Reduced focal ERG	34	2					
Normal focal ERG	9	48					
			79	96	89	51.8	≤0.001
Implicit time							
Delayed focal ERG	20	2					
Normal focal ERG	23	48					
			46	96	73	20.8	≤0.001
Combined amplitude/implicit time							
Reduced/delayed focal ERG	37	4					
Normal focal ERG	6	46					
			86	92	89	54.0	≤0.001

ERG = electroretinogram.

vision not due to maculopathy, focal ERG amplitude yielded a positive result in only two eyes and a negative result in the remaining 26 eyes. Thus, the specificity rate was 93%, indicating few false-positives. The overall accuracy rate of focal ERG amplitude in detecting maculopathy in eyes with reduced vision was 87%. Implicit time was normal in the majority of eyes with maculopathy and less than 20/40 visual acuity (Table 6, center) with a sensitivity rate of 39%. However, combining amplitude and implicit time criteria (Table 6, bottom) increased sensitivity rate to 91% and overall accuracy rate in detecting maculopathy to 91%.

Eyes with reduced acuity (macular holes excluded). Because of the poor correlation between focal ERG amplitude and Snellen acuity in eyes with macular holes, a separate analysis was done for the group of eyes with reduced vision excluding macular holes (Table 7). In these 68 eyes, the sensitivity and the accuracy rates of the amplitude criterion were improved to 90%. Combining amplitude and implicit time criteria (Table 7, center) led to a sensitivity rate for detecting maculopathy of 94% and an accuracy rate in discriminating causes of visual loss of 94%.

DISCUSSION

A correlation has previously been established between the amplitude of the foveal focal ERG and Snellen acuity in eyes with maculopathy excluding macular holes.[4,11,12] In the current study, the relationship between log Snellen acuity and log focal ERG amplitude was examined in three groups of patients: (1) the entire group of eyes including those with macular holes, (2) the eyes with macular holes, and (3) eyes with maculopathy excluding macular holes. A low correlation between log Snellen acuity and log focal ERG was found in the eyes with macular holes. This may be due to the relatively large size of the focal stimulus compared with the size of some of the smaller macular holes. Despite significant visual reduction

Table 6. Focal Electroretinogram versus Maculopathy in All Eyes with Less Than 20/40 Snellen Acuity

	No. of Eyes		Sensitivity (%)	Specificity (%)	Accuracy (%)	Chi-square	*P*
	Maculopathy	No Maculopathy					
Amplitude							
Reduced focal ERG	94	2					
Normal focal ERG	16	26					
			86	93	87	61.0	≤0.001
Implicit time							
Delayed focal ERG	43	0					
Normal focal ERG	67	28					
			39	100	51	14.1	≤0.001
Combined amplitude/implicit time							
Reduced/delayed focal ERG	100	2					
Normal focal ERG	10	26					
			91	93	91	76.9	≤0.001

ERG = electroretinogram.

Table 7. Focal Electroretinogram versus Maculopathy in All Eyes with Less Than 20/40 Snellen Acuity Except Those with Macular Holes

	No. of Eyes		Sensitivity (%)	Specificity (%)	Accuracy (%)	Chi-square	*P*
	Maculopathy	No Maculopathy					
Amplitude							
Reduced focal ERG	61	2					
Normal focal ERG	7	26					
			90	93	90	56.3	≤0.001
Implicit time							
Delayed focal ERG	29	0					
Normal focal ERG	39	28					
			43	100	59	15.1	≤0.001
Combined amplitude/implicit time							
Reduced/delayed focal ERG	64	2					
Normal focal ERG	4	26					
			94	93	94	65.8	≤0.001

ERG = electroretinogram.

in these eyes, if enough functional cones remain, the focal may be normal. The best correlation was found in the group of eyes with maculopathy excluding macular holes, but variability precluded accurately indexing the focal amplitude with Snellen acuity.

Focal cone ERG amplitude was 82% accurate in discriminating eyes with macular disease from eyes with visual acuity loss due to other causes. Although assessment of eyes with dense cataracts could be compromised on optical principles alone, the specificity rate of focal ERG amplitude (96%) in this group was equivalent to that expected in a random sample of normal eyes.

The diagnostic value of the focal ERG was improved when an implicit time criterion was considered along with an amplitude criterion. As reported previously,[12] some patients with macular disease and borderline normal amplitudes show significant delays in implicit time. Using both amplitude and implicit time criteria, the overall sensitivity in detecting maculopathy among all eyes with maculopathy was 85%. The sensitivity rate was lower (66%) in the eyes with good vision. Many patients with normal acuity, but with maculopathy, showed abnormal focal ERGs. A relatively small number of healthy cones in the foveola may be sufficient to support good acuity, whereas a normal focal ERG may require healthy cones throughout much of the central 3°. Alternatively, functionally abnormal cones may be able to respond to steady, high contrast Snellen letters while being relatively less responsive to flickering stimuli. As a precataract potential visual acuity test, however, this group with good vision and reduced focal amplitudes would be considered as false-positives since the standard is visual acuity rather than the presence of maculopathy.

Log focal ERG amplitude was not significantly correlated with log Snellen acuity in eyes with macular holes. Nevertheless, the focal ERG had a sensitivity rate of 86% in detecting maculopathy in eyes with macular holes, a detection rate similar to that in all eyes with maculopathy. However, since virtually all macular holes had reduced vision, the comparable group contains the eyes with re-

duced vision due to other forms of maculopathy. In this group, the sensitivity rate of detecting maculopathy was 94%, which compares favorably with the 91% sensitivity rate previously reported in a smaller group of eyes.[5]

Salzman et al[18] showed a reduction in focal ERG amplitude (40 Hz) in 43% of 23 eyes with aphakic cystoid macular edema (CME) and reduced vision. Our series includes one eye with CME and reduced vision which had normal focal amplitudes. Thus, cystoid macular edema would appear to be another cause of maculopathy which is difficult to detect with the focal ERG. Perhaps the relative lack of permanent tissue alteration in some cases of CME allows the focal ERG to maintain normalcy.

An important consideration in precataract evaluation is to rule out the eye with maculopathy which will have very poor, nonreading vision. In this series, 6 of 78 eyes (8%) with 20/80 or worse visual acuity had a normal focal ERG. Five of these six eyes had a macular hole as the cause of acuity loss. Omitting these, only one eye with a normal focal ERG had 20/80 or worse visual acuity, an eye with macular pigment epithelial atrophy due to dry age-related macular degeneration. Therefore, a normal focal ERG has a low failure rate (excepting macular holes) in ruling out eyes with maculopathy causing less than 20/80 visual acuity. This compares favorably with other macular function tests.[5,19-26]

The results also showed that eyes with low focal ERG amplitude are unlikely to have good Snellen acuity. In a total of the 51 eyes with a focal amplitude of 0.1 μV or less, only four eyes (8%) had 20/40 or greater visual acuity. These included one eye each with retinitis pigmentosa and hereditary macular degeneration, and two eyes with dry age-related macular degeneration. All had variable acuity and were severely handicapped although under optimal circumstances could achieve 20/40 visual acuity due to remaining cones in the macula. Therefore, a focal 0.1 μV or less strongly suggests compromised macular function assuming the media clarity is sufficient for testing.

In summary, the focal ERG is a highly sensitive direct measure of maculopathy as a cause of reduced acuity. There is a significant inverse correlation between log focal ERG amplitude and log Snellen acuity in eyes with maculopathy, except in those eyes with macular holes. The focal may prove useful as a presurgical test in eyes with moderately opaque media. However, eyes with maculopathy, which reduces vision yet with a relatively large number of functioning cones (i.e., macular holes), may have a normal focal ERG.

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