Volume 1 Number 12 1981/1982

Current Eye Research

Temporal factors in the foveal ERG

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Received 8 February 1982; accepted 9 June 1982

ABSTRACT

Peak latencies of the foveal (4° diameter) ERG and the sensitivity of the technique in various diseases have been investigated. The method previously reported (1) uses a rapidly flickering red test light against a white surround of rod saturating luminance. Control ERG's from the same stimulus are also recorded from blind spot stimulation. In senile macular degeneration the sensitivity limit of the test is about 20/60 acuity.

New findings include:

(1) In senile macular degeneration, the foveal ERG peak latency is usually not abnormally delayed (only 7% of 30 eyes delayed).

(2) In contrast, in Stargardt's macular dystrophy, the foveal ERG peak latency is frequently abnormally delayed (47% of 34 eyes). Even at 20/20 to 20/30 acuity, the majority of eyes with Stargardt's have either delayed peak latency, abnormal amplitude or both.

(3) In retinitis pigmentosa the sensitivity limit of the foveal ERG (amplitude ratio) is 20/30 to 20/40 (29 eyes). Peak latencies were delayed in 31% of the eyes.

INTRODUCTION

A local electroretinogram from the central macular region (foveal ERG) has been used to detect local cone function in a variety of diseases. The standard photopic ERG cannot evaluate foveal cone function due to the relatively small number of cones in the foveal region compared to the entire retina. The foveal ERG technique requires a highly light-adapted surround to reduce stimulation by scattered light and computer averaging to reveal the very small ERG from the fovea (1). The technique has proven useful in a variety of diseases including: macular degeneration (1-4), Best's dystrophy (1,5), central serous retinopathy (6), central areolar choroidal sclerosis (7), as well as several others (5,8). Most previous studies have looked only at the amplitude of the foveal ERG. In this study, the temporal aspects of the foveal ERG in addition to its amplitude have been investigated (9). Patients with Stargardt's dystrophy, senile macular degeneration, and retinitis pigmentosa were studied.

METHODS

The method used here was similar to that previously used in a standardization series on patients mostly with macular degeneration (1). The technique utilizes a hemispherical surround illuminated with a white light at a high intensity of 300 footlamberts, above the saturation value for the retinal rods. This minimizes stimulation of non-focal retina by stray light from the stimulus. Instead of the single adaptation bulb used in the original study, 3 tungsten-iodide bulbs all with ultraviolet and heat rejection filters illuminated the surround in this study. At the center of the hemisphere, an aperture of 4 degrees diameter admitted the flashing stimulus light from a Grass photic stimulator through a diffusor and a red glass filter (Corning 2424). According to the manufacturer, the Grass photic stimulator at intensity 8 produces a flash of 750,000 candlepower lasting approximately 10 microseconds. The diameter of the illuminated surround was 50 degrees. The patient was seated at the hemisphere with his face supported on an ophthalmic chin rest. Since many patients with a central scotoma are unable to fixate their eye on the four degree target, wide black horizontal and vertical lines were provided which intersected at the fixation point and extended to the limits of the illuminated surround. Fixation points were thus provided at the four degree central aperture and at 15 degrees to the right and 15 degrees to the left of center.

As the focal electroretinogram from a 4 degree

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area is quite small (1 to 5 microvolts), computer averaging of the response was necessary. A Hewlett Packard digital signal analyzer was used, and 512 sweeps were averaged. The electroretinogram was recorded with a Riggs contact lens with chlorided silver electrode. Other chlorided silver electrodes were attached to the face and to the mastoid for ground. An oscilloscope provided monitoring of the eye responses, and permanent records of the analyzer output were produced by an x-y recorder. Flicker stimulation was used at a rate of 18 Hertz. A relatively rapid flicker rate was used (a) to reduce rod responsiveness to the test flashes, and (b) to get a large number of averaged ERG's within a minimum time to reduce patient fatigue and wandering fixation. Upper limits on the flicker rate were dictated by the power output of the photic stimulator. An artefact rejection circuit, added since the initial paper, eliminated averaging of sweeps contaminated by blinks or large eye movements.

For most of the patients tested, amplifer band pass (simple RC filter) was from 0.2 to 100 Hertz. As the high frequency limit of the amplifiers is reduced, the peak latency of the ERG increases. The latencies in this paper are specific to this high frequency limit.

Patients were referred through the University Ophthalmology Clinics, previously at the Ohio State University and currently at the University of South Florida. Corrected visual acuities were recorded. In the present data only eyes with clear optic media have been included. Pupils were not dilated.

After attachment of the electrodes and insertion of the contact lens, the eye not being tested was covered with an eye-patch. The ERG was recorded with the four degree red test stimulus at the fovea, and then at the optic disc. Three intensity settings on the photic stimulator were used; 4, 8, and 16. In order to control for adequacy of fixation and light scatter, the ratio of the ERG amplitude at the fovea to that at the optic disc was calulated. The average of the ratios at each of the three settings is the value reported. Average latencies to the b wave peaks (implicit time) were also recorded.

At the same session, the photopic ERG was also recorded in a ganzfeld (integrating sphere) with steady white illumination at 20 foot-lamberts. A Grass photic stimulator bulb above the patient's head illuminated the inside of the sphere evenly with white flashes to produce full retinal stimulation. Computer averaging of the ERG at a 9 Hertz flicker rate was used.

A control group of older (mean age 51 years) volunteer normal subjects was tested with the procedures to establish normal values. Control eyes had corrected visual acuities of 20/20 or better and no ophthalmoscopic evidence of eye disease.

RESULTS

Figure 1 shows representative local ERG's (4^{o} diameter) obtained from the fovea and optic disc of a patient with senile macular degeneration as compared with a normal eye. The normal older control eyes (ten) had a mean foveal ERG peak latency of 33.2 milliseconds and a standard deviation (SD) of 3.4 milliseconds. Abnormal delay was taken as greater than the mean plus two SD or 40.0 milliseconds. This control was used for all three groups of patients due to the large number

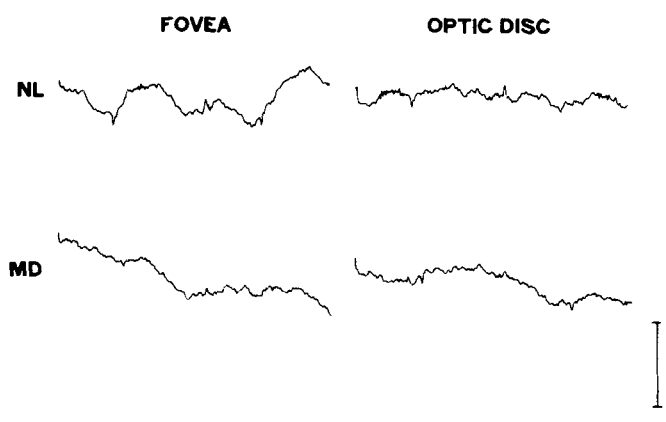

Fig. 1 Four degree diameter ERG's at the fovea and at the optic disc for a normal eye (upper row) and a senile macular degeneration (CF acuity) (lower row). Intensity 8. Trace length 100 milliseconds. Calibration 5 microvolts. Two ERG's in each trace.

of older patients in all groups. The younger control group (mean age 30 years) previously used (1) had a mean foveal ERG peak latency of 32.4 milliseconds and a SD of 3.1 milliseconds. Foveal ERG's, both normal and abnormal, frequently had double peaks, although a single peak was more common. The highest amplitude peak was the one utilized in the analysis.

The photopic ERG peak latencies from the older control eyes had a mean of 26.0 milliseconds with a SD of 2.6 milliseconds. Thus the normal mean foveal peak latency was longer than the mean photopic peak latency.

The eyes with senile macular degeneration (SMD) had changes varying from fine stippled pigmentary disturbances in the macula to more advanced irregular pigment clumping. The visual deficit sometimes varied considerably from the ophthalmoscopic appearance. The mean age was 57 years with a SD of 11 years. Of the photopic ERG's in the eyes with SMD, 60% were normal, 30% borderline, and 10% abnormal.

Foveal ERG's of the patients with SMD were often reduced in amplitude, but were not usually delayed from the normal foveal ERG peak latency. The amplitude cut-off ratio for abnormal foveal ERG's in the previous paper (1.50) was also used here. Of the 16 eyes in the present study, 9 foveal ERG's were abnormal in amplitude ratio while 1 was abnormally delayed. Of the 14 eyes in the previous study (1), 10 foveal ERG's were abnormal in amplitude ratio while 1 was abnormally delayed. The visual acuity at the cut-off ratio was similar in both samples. As the two samples appeared quite similar in all respects, they were combined, and the amplitude ratios of the 30 eyes are presented in Fig. 2. A dashed horizontal line marks the cut-off ratio of 1.50. Eyes with poor acuity have ratios less than that, with an asymptote at the noise level of 1.00. The ratio 1.50 provides an acuity sensitivity of about 20/60 for the foveal ERG in macular degeneration. Patients with acuities better than 20/60 may or may not have an abnormal foveal ERG. The amplitude results confirm those of the earlier paper (1).

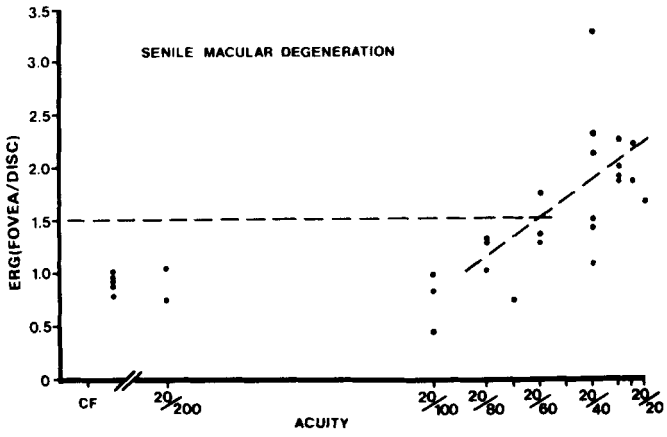

Fig. 2 Foveal ERG ratio vs. visual acuity for eyes with senile macular degeneration. Horizontal line at 1.50 cut-off value. Sloped line for acuities above cut-off at 20/60.

From the 39 eyes, only 2 foveal ERG's were abnormally delayed (7%).

Another disease investigated with the foveal ERG was retinitis pigmentosa. Most of the retinitis pigmentosa patients (22 of 29 eyes) had typical pigment deposits and attenuated retinal vessels. Some had clinically evident macular pathology. The ones without pigment deposits were clinically diagnosed on other standard criteria. All eyes had abnormal scotopic ERG's. The photopic ERG's in two eyes were normal, borderline in three eyes, and abnormal in the others.

Figure 3 presents the foveal ERG amplitude ratios on the sample of 29 eyes with retinitis pigmentosa (mean age 32 years, SD 19 years). The same cut-off ratio of 1.50 is used. With retinitis pigmentosa, the foveal ERG was more sensitive to visual acuity decrease in this sample than it was for senile macular degeneration. The amplitudes drop rapidly as acuity decreases with cut-off between 20/30 and 20/40. Foveal ERG peak latencies were frequently delayed in retinitis pigmentosa. Nine eyes (31%) had delayed foveal ERG's. Thirteen eyes came from patients with negative family histories, of which 38% were delayed. Of 8 eyes with dominant inheritance, only one foveal ERG peak latency was delayed (Sector RP). The remaining eyes were of other or unknown inheri-

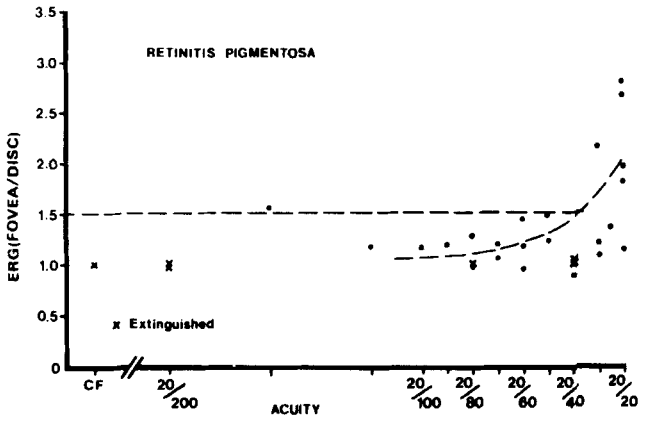

Fig. 3 Foveal ERG ratio vs. visual acuity for eyes with retinitis pigmentosa. Horizontal line at the 1.50 cut-off value. Curved line for acuities above cut-off at 20/30-20/40.

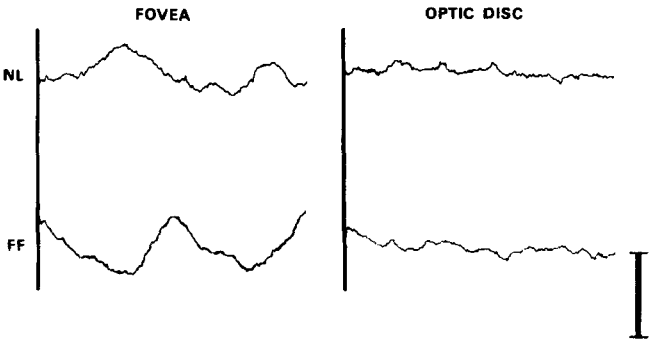

Fig. 4 Four degree diameter ERG's at the fovea and at the optic disc for a normal eye (upper row) and a Stargardt's dystrophy (20/20 acuity) (lower row). Intensity 8. Trace length 100 milliseconds. Calibration 5 microvolts. Two ERG's in each trace. Foveal peak latency normal - 32 milliseconds, Stargardt's - 50 milliseconds.

tances.

The third disease reported on here is Stargardt's dystrophy (fundus flavimaculatus). These patients were all in Group II (with atropic macular degeneration) of Krill and Deutman (10) except one patient (two eyes) who fell in Group I (without macular degeneration). Of the Group II eyes, 26 fell in subgroup A (no evidence of diffuse cone abnormality) with normal photopic ERG's. Eight eyes fell in subgroup B with borderline or abnormal photopic ERG's. Twenty-two eyes had abnormal electro-oculograms and two were not tested. The mean age was 32 years with a SD of 12 years.

The foveal ERG's in the Stargardt's patients were more variable than in the other two diseases with patients of normal acuity usually showing abnormal amplitudes or delayed peak latencies. Figure 4 illustrates foveal ERG's from a normal eye, and one with Stargardt's macular dystrophy. Both eyes had 20/20 acuity. Both eyes had normal amplitude ratios (the optic disc responses being quite low), but the Stargardt's eye had a grossly delayed foveal ERG. Table 1 gives the frequencies of both abnormalities in our sample of 34 eyes with Stargardt's dystrophy.

Even at 20/20-20/30 acuity, an eye with Stargardt's had a 64% chance of either abnormal delay or amplitude. When acuity was 20/40 or worse 100% of the foveal ERG's showed either abnormal delay or amplitude. Of the 34 eyes, 16 had delayed foveal ERG's (47%). No relation between abnormality of the foveal ERG and the distinction between subgroups A and B was seen.

Table 1: Foveal ERG's in Stargardt's Dystrophy

Acuity	Number of Eyes	Abnormal Amplitude	Abnormal Latency	Abnormal Amplitude or Latency
20/20	7	57%	29%	86%
20/30	7	43	29	43
20/40	3	67	100	100
20/50-20/60	7	86	29	100
20/80-20/100	3	100	33	100
20/200	4	75	100	100
CF	3	100	67	100
Total	34	71%	47%	85%

DISCUSSION

Obviously the foveal ERG is not a direct measure of visual acuity, but rather is a measure of light responsiveness of the foveal retina. Nevertheless, with proper controls to minimize extra-

macular scattered light, it correlates fairly well with retinal visual acuity in a clinical test. The size of the central test stimulus has varied in different studies. A diameter of 2^{o} to 4^{o} seems to be about the minimum to get reliable responses with average clinic patients. A larger stimulus such as 10^{o} produces larger ERG's, but is less well correlated with visual acuity (11). Because the foveal ERG is a measure of light responsiveness and not a direct measure of visual resolution, it can be tested without refractive correction and still maintain its correlation with best acuity. There are other techniques for recording a local ERG such as alternating pattern which have not yet been correlated with organic acuity deficits (12).

The present data show a longer mean peak latency for the foveal than the photopic ERG. Of course, the test conditions differ somewhat, so that research with conditions matched as closely as possible is necessary to confirm that foveal cones truly have a longer response time than peripheral cones. This type of research has been done by Brindley and Westheimer (13). In Figures 8 and 11 of that paper, the foveal ERG (2^{o} -4^{o} diameter) has a longer peak latency and a tendency toward multiple peaks. When the stimulus becomes as large as 10^{o} diameter the ERG has lost its foveal character and its peak latency is not different from the peripheral ERG (Figures 3 and 11). There is some evidence that the foveal cones also have a longer response time in dark adaptation. In a psychophysical study of dark adaptation, Norren and Padmos found a longer time constant for the foveal R-G cones than for the extrafoveal R-G cones (14).

The present data with a similar technique and a larger sample confirm the previous study showing the sensitivity of the foveal ERG in senile macular degeneration to be about 20/60 in visual acuity (1). The present study also indicates that a minority of eyes with SMD (7%) have an abnormally delayed foveal ERG.

In contrast, many eyes with Stargardt's dystrophy do have abnormally delayed foveal ERG's (47%). This finding, together with the frequently abnormal EOG, suggests a different retinal defect than that occuring in senile macular degeneration. Clinically, the different pattern of results helps establish the diagnosis. Also the high percentage of abnormal foveal ERG's even with good acuity in Stargardt's dystrophy makes the test very useful clinically. Subnormal amplitudes of foveal ERG's in Stargardt's dystrophy have been reported by Deutman (5) and Bankes (3). Sandberg et. al. (15) have reported that patients with juvenile macular degeneration often have delayed and reduced amplitude foveal ERG's.

A number of recent studies have shown macular fluorescein patterns to be abnormal in retinitis pigmentosa. At 20/30 or 20/40 acuity, the present data show the foveal ERG to be significantly abnormal. This is consistent with the study by Krill et. al. (16) who found in a study of retinitis pigmentosa that every patient with 20/40 or worse acuity had an abnormal fluorescein angiogram in the macula. Also Sandberg et. al. reported abnormal foveal ERG's in retinitis pigmentosa at 20/40 or poorer acuity (15). The latter author's finding of normal foveal ERG peak latencies in retinitis pigmentosa contrasts with the present finding of 31% delayed latencies. The reason for this difference is unknown. Retinitis pigmentosa is a heterogeneous disease, however, and of the patients with negative family histories in this study, 38% had delayed latencies, while most of those with dominant inheritance had normal peak latencies.

The present technique is limited to use on cooperative patients who are able to fixate where directed. Generally patients old enough to wear the contact lens (e.g. 6-8 years) are also able to fixate where directed unless they have nystagmus. Patients with nystagmus cannot be tested. The technique is not useful for detection of malingerers or where eccentric fixation ($>2^{o}$) is suspected. For such patients a method allowing experimenter monitoring of fixation would be better, such as the stimulator-ophthalmoscope of Sandberg et. al. (15). Most patients with acuity reduced to the finger counting level can be tested with the pre-

sent fixation aids provided by the wide black lines.

The selection of the amplitude cut-off ratio used (1.50) was discussed in the previous paper and involved the balancing of Type I vs. Type II errors on the patients as well as comparison with normals (1). One advantage of a ratio over an absolute amplitude is that the former is insensitive to pupil size. Patients with extreme miosis can be dilated; however, the intensity of the adapting illuminants should be reduced if such is done.

This research shows that abnormal foveal ERG's are found in senile macular degeneration, Stargardt's dystrophy, and retinitis pigmentosa. In other studies, abnormal foveal electroretinograms have now been described in Best's dystrophy, juvenile retinoschisis, progressive foveal dystrophy, central serous retinopathy, and central areolar choroidal sclerosis. The foveal ERG measures of both amplitude and peak latency are useful additions to the clinical battery of electrophysiological tests.

ACKNOWLEDGEMENTS

This study was supported in part by Research Grants EY00454 and EY03155 from the National Institutes of Health.

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