Normal Change in the Foveal Cone ERG with Increasing Duration of Light Exposure

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Foveal cone electroretinograms (ERG) were elicited with a stimulator-ophthalmoscope from 24 normal subjects with a 4° stimulus flickering at 42 Hz and centered within a 12° steady surround. The stimulus and surround were presented at retinal illuminances of 4.8 log td and 5.5 log td, respectively, to facilitate visualization of the fundus. Several consecutive averaged responses were evaluated to determine whether increasing duration of light exposure causes an increase in amplitude, as previously found for the full-field cone ERG. On average, amplitude increased by 27% over time, and the linear regression of amplitude on recording number accounted, on average, for 42% of the amplitude variability between consecutive responses. Two subjects had amplitudes that were initially subnormal, based on previously published norms, but that value increased to within the normal range in subsequent recordings. These findings show that a significant change in the cone ERG occurs in the fovea with increasing duration of light exposure at these retinal illuminances, and suggest that, when the stimulator-ophthalmoscope is used, consecutive foveal cone ERGs should be obtained from patients with suspected macular disease to avoid a false diagnosis of retinal malfunction. Invest Ophthalmol Vis Sci 32:2842-2845, 1991

Foveal cone electroretinography has been used by various centers over the last 25 yr to detect macular malfunction and to supplement information obtained from funduscopy and fluorescein angiography. Since 1977, this approach has been combined in some centers with ophthalmoscopic viewing of the fundus, using visible light, as a way to ensure that the stimulus is centered on the fovea throughout testing, even in patients with variable or eccentric fixation. While using such instrumentation, ie, a stimulator-ophthalmoscope, we have observed a tendency for foveal response amplitude to increase during continued testing in some subjects. This increase is reminiscent of increases in amplitude in the full-field cone electroretinogram (ERG) which reflects primarily extravesical cone function. This study was done to determine whether foveal cone ERGs elicited with a stimulator-ophthalmoscope change systematically with increasing duration of light exposure in normal subjects and, if so, to quantify the magnitude of this effect as it may bear upon response variability and the clinical assessment of foveal function.

Subjects and Methods. Foveal cone ERG responses were evaluated retrospectively from 24 consecutive normal subjects (range: 8–60 yr) who participated as volunteers (15 subjects) or were patients referred with a question of reduced vision but had visual acuities of 20/25 or better and no abnormalities detected by visual field, color vision, dark adaptation, full-field or focal electroretinography, or ophthalmoscopy (9 subjects). All subjects gave informed consent before they were tested. They were maintained in ambient room illumination with dilated pupils before testing in accordance with our routine diagnostic protocol. Testing was done by one or the other authors. Both were experienced in focal cone electroretinography with the methods described below. Recordings were obtained in a dimly lit room with a hand-held, dual-beam stim-
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Fig. 1. Foveal cone ERG amplitude vs recording number in three representative normal subjects (left) and in two normal subjects who showed subnormal amplitudes at baseline (right). Responses were elicited with a stimulator–ophthalmoscope. Recording periods lasted 15–60 sec and were separated by 30-sec intervals in the dark.

... Responses were elicited with a 4° white stimulus flickering (50% duty cycle) at 42 Hz at a retinal illuminance of 4.8 log td (mean retinal illuminance: 4.5 log td). The stimulus was positioned on the fovea and centered within a 12° white, steady surround of 5.5 log td.

Responses were monitored with a bipolar Burian–Allen contact lens electrode on the topically anesthetized cornea. Signals were differentially amplified, smoothed by a narrow bandpass filter tuned to 42 Hz, and summed by a signal-averaging computer containing an artifact reject buffer that eliminated voltage deflections of >5 μV due to eye or lid movements. Testing involved consecutive recording periods that lasted from 15–60 sec each (depending on response phase reliability) and were separated by 30 sec in the dark for data transfer, display and storage on disk by a personal computer (Macintosh SE, Apple Computer, Cupertino, CA). Responses, which appeared sinusoidal, were quantified by Fourier analysis with respect to amplitude and implicit time, ie, interval from stimulus onset to the corresponding cornea-positive response peak, and these values were printed to the screen. In all cases, at least three recordings were made, usually until responses had stabilized. Stabilization occurred if the last recording showed a change in amplitude opposite in direction to the prior trend and an amplitude and implicit time that were not different from those of the previous response by more than 10% and 1 msec, respectively.

In addition to the above protocol, five normal subjects were tested prospectively in a dark room, after 45 min of dark adaptation and 5 min of adjustment to the contact lens electrode. Subjects were tested for at least 9 min and until response stabilization was evident. One of the authors positioned the stimulus and surround on the macula, centered on the fovea, within 10–15 sec of illuminating the retina, and maintained its location during both recording and data analysis periods. The data were transferred, displayed, and stored by the other author. Four of the five subjects had prior experience as subjects for focal ERG testing.

Results. Foveal cone ERG amplitude increased in 21 subjects (Figure 1), remained unchanged in 1 subject, and decreased slightly in 2 subjects over consecutive recordings under the conditions of our routine diagnostic protocol. Based on finding from all 24 subjects, mean change in amplitude between the first and third recordings was +27% (t = 3.64 based on log data, P = 0.001). Linear regression of amplitude vs recording number accounted, on average, for 42% of the amplitude variability between consecutive responses. Two of the subjects had amplitudes that were subnormal at baseline (< 0.18 μV) based on a previously published lower limit of normal, but that value increased to within the normal range by the second recording (Fig. 1, right). The amplitude change between the first and third recordings was inversely related to baseline amplitude (P = 0.006); subjects with smaller baseline amplitudes tended to show larger relative increases (Fig. 2). Foveal cone ERG implicit time...
increased over sequential recordings in 21 subjects, remained unchanged in 2 subjects, and decreased in 1 subject. Based on all 24 subjects, the mean change between the first and third recordings was +0.7 msec (t = 3.27, P = 0.003). Change in implicit time was not significantly related to baseline implicit time for this sample size.

For the five subjects who were tested prospectively, amplitude data were each fitted to a second-order polynomial as a function of time of light exposure. Initial and final amplitudes were derived from the fitted curves for time points that represented 30 and 460 sec, respectively. Mean change in amplitude was +34%, not significantly different from the +27% seen in the retrospective analysis on 24 subjects. Two of the five subjects tested prospectively were also among those whose ERG findings were evaluated retrospectively, and their increases in amplitude were remarkably similar retrospectively vs prospectively (32% vs 30% and 3% vs 3%, respectively).

Discussion. This study shows that, on average, a substantial increase in amplitude (27%) and a small increase in implicit time (<1 msec) occurred in the foveal cone ERG recorded from 24 normal subjects, using a stimulator-ophthalmoscope, with increasing duration of light exposure. Response amplitude typically increased over several recordings before it stabilized. This amplitude change in the foveal ERG with increasing duration of light exposure cannot be attributed to such factors as stimulus localization on the fovea or adjustment of the subjects to the contact lens electrode; both examiners were well trained in foveal ERG testing and stimulus localization, and normal subjects have no difficulties fixating at the center of the stimulus throughout testing. Furthermore, in the prospective study, subjects were given 5 min to adjust to the contact lens electrode before recording and still showed the increase in amplitude over time.

The amplitude increase at the fovea is reminiscent of that which occurs in the full-field cone ERG with increasing exposure to lower retinal illumination.9,10 The physiologic basis for either of these effects is not known. Interactions between cones and rods or within the cone system itself have been suggested as mediating flicker detection in the fovea depending on background brightness; the retinal illuminances used in this work (>2 log td) appear to favor an effect that involves only cones.11 The foveal ERG amplitude increase was smaller, on average, than the 60–75% increase seen in the full-field cone ERG,9,10 which could reflect a regional variation. However, several differences exist between our routine diagnostic method of focal testing and that used in full-field studies, these differences may account for the smaller effect seen in the foveal ERG. One difference is the higher cone pigment bleach caused by the retinal illuminance of our focal stimulus (ie, ~75%13) compared with that produced by the lower retinal illuminances of conventional full-field stimulation (ie, < 10% bleach13). The bleach from the focal stimulus, which would take 1–3 min to reach steady state with continuous stimulation, may partially negate the mechanism underlying the increase in amplitude by progressively reducing quantum catch. Another difference is the 15–60 sec averaging that is necessary to determine amplitudes of less than 1 µV, and that which may have artificially limited the range of change seen in the foveal response. Two other differences in methodology—the fact that subjects were maintained in ambient room illumination before they were tested and the use of 30-sec dark intervals between successive recordings for data analysis, display, and storage—do not appear to have been factors, because subjects tested prospectively after full dark adaptation and with continuous light exposure showed an average increase in amplitude comparable to that seen with our routine diagnostic protocol.

Our practice in quantifying foveal function in pa-
patients with known or suspected macular disease is to record consecutive responses to show waveform reproducibility. These findings suggest that repeated recordings should be performed to allow for any changes that may be related to increasing duration of light exposure. Because the increase in amplitude was greatest for subjects with the smallest initial amplitudes and because two of our normal subjects had amplitudes that fell below the normal range initially, we suggest obtaining several consecutive recordings in patients who show a subnormal amplitude to determine whether foveal function is subnormal.

Key words: cone, electroretinogram, fovea, light exposure, macular malfunction

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References