Principles and Practice of Clinical Electrophysiology of Vision

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Flicker Electroretinography

David G. Birch

Virtually all clinical electroretinogram (ERG) protocols, including that endorsed by the International Society for Clinical Electrophysiology of Vision and the National Retinitis Pigmentosa, Inc., utilize a 30-Hz flickering stimulus to elicit an isolated cone response. Because of their low temporal sensitivity, rods are unable to follow frequencies above approximately 15 Hz.[9] Typical flicker responses from a normal subject are shown in Figure 45–1,A. Vertical spikes indicate each 10-μs flash. Cone b-wave implicit time is the time interval between flash onset and the major cornea-positive peak (horizontal arrow). Peak-to-peak amplitude is measured from the cornea-negative peak to the succeeding cornea-positive peak (vertical arrow). Implicit time and amplitude can vary independently. As shown in Figure 45–1,B, progressive forms of retinal degeneration such as retinitis pigmentosa typically lead to a substantial delay in cone b-wave implicit time.[3–5] Diseases that affect regional or localized areas of retina typically lead to decreased amplitude without necessarily affecting the cone b-wave implicit time (Fig 45–1,C).[5, 6]

Flickering stimuli and the resulting "steady-state" ERG permit extensive use of analog and digital flickering techniques. As shown in Figure 45–1,D, many patients with retinitis pigmentosa show no response to flicker with traditional computer-averaging techniques. Band-pass amplification (tuned to the stimulus frequency) or digital filtering can be used to enhance the signal-to-noise ratio of very small signals.[1] When only that portion of the response that is time locked to the stimulus is amplified (Fig 45–1,E), the noise level drops to approximately 0.1 μV as compared with a noise level of approximately 2.0 μV without band-pass amplification.

The ERG to stimuli flickering at 30 Hz is an important diagnostic indicator, with two protocols in common use. Some laboratories obtain the response following 45 minutes of dark adaptation. The response is obtained with a medium-intensity white stimulus (i.e., Grass setting 4 or 8) to minimize patient discomfort and avoid the irregular behavior of the photostimulator at the highest setting. Since cone responses typically grow in amplitude during the first few minutes of light adaptation,[8] the patient should be pre-exposed to the flickering stimulus before recording the flicker response. The second protocol involves recording the flicker response in the presence of a steady background (typically 10 foot-lamberts [ft-L]) after at least 10 minutes of light adaptation. The two protocols differ primarily in the degree of light adaptation. The time-average retinal illuminance of 30-Hz flicker without a steady background is typically about 2.8 log photopic troland-seconds (phot td-sec). The addition of a steady background of 10 ft-L raises the mean retinal illuminance to 3.4 log phot td-sec. We compared the two protocols in 10 normal subjects and 33 consecutive patients with retinitis pigmentosa (unpublished observations). In both normals and patients, the addition of a steady background lead to a shortening of cone

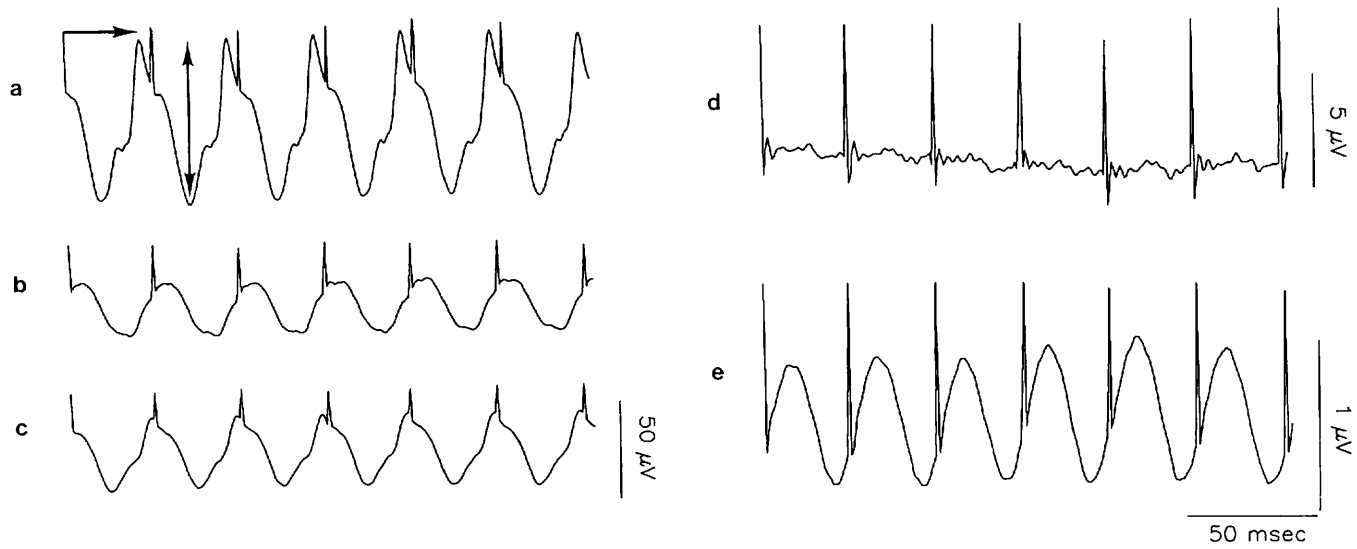

FIG 45–1.
Flicker responses to 30-Hz stimulation. The spike artifact indicates stimulus flash. A normal subject has a b-wave implicit time of 29 ms **(A).** The response is reduced in amplitude and delayed in retinitis pigmentosa **(B)** but reduced with normal timing in presumed histoplasmosis **(C).** Even with extensive averaging, the response is nondetectable in many patients with retinitis pigmentosa **(D).** A band-pass amplifier tuned to the stimulus frequency selectively enhances time-locked activity to reveal a small response **(E).**

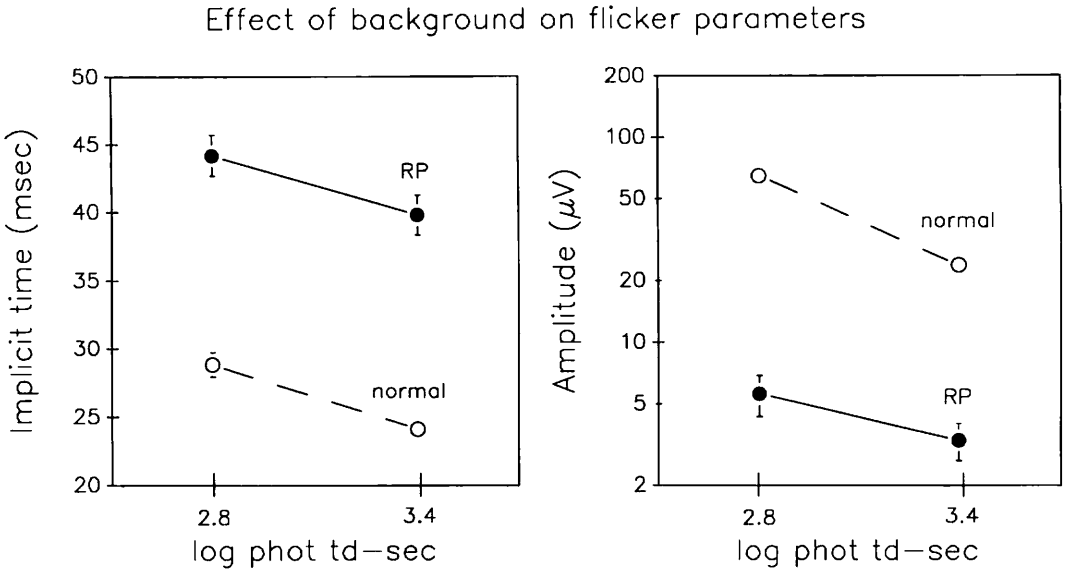

FIG 45–2.
Cone b-wave implicit time (±1 SE) and cone b-wave amplitude (±1 SE) at two background levels in 10 normal subjects and 33 consecutive patients with retinitis pigmentosa. The lower background level is the time-average retinal illuminance of the 30-Hz white flashes. The higher background level is the mean retinal illuminance of the flicker superimposed on a steady (10 ft-L) background. Both normals and patients show a decrease in implicit time of approximately 4 ms and a decrease in amplitude of approximately 50% at the higher adaptation level.

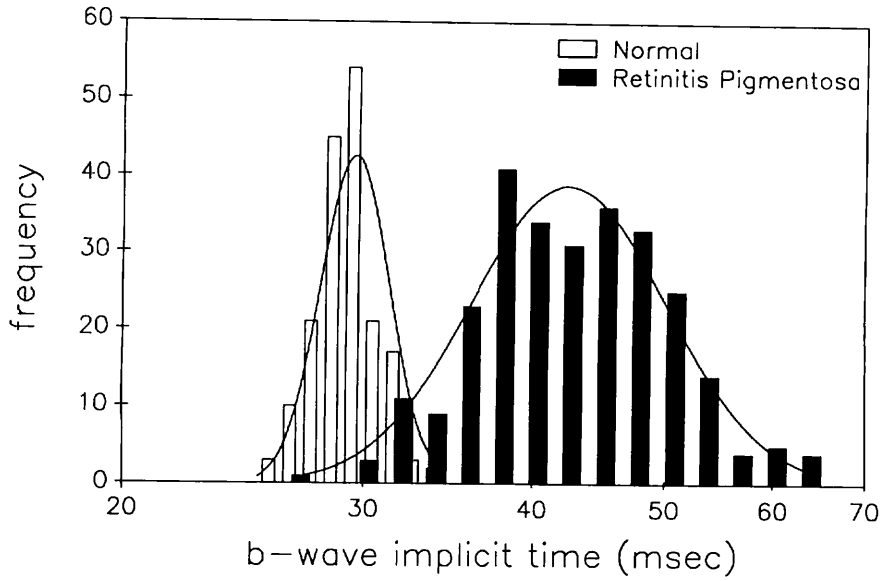

FIG 45–3.
Cone b-wave implicit time distributions for 30-Hz flicker in 175 normal subjects and 250 patients with retinitis pigmentosa (excluding autosomal dominant disease). Both distributions are plotted in logarithmic units and are normally distributed.

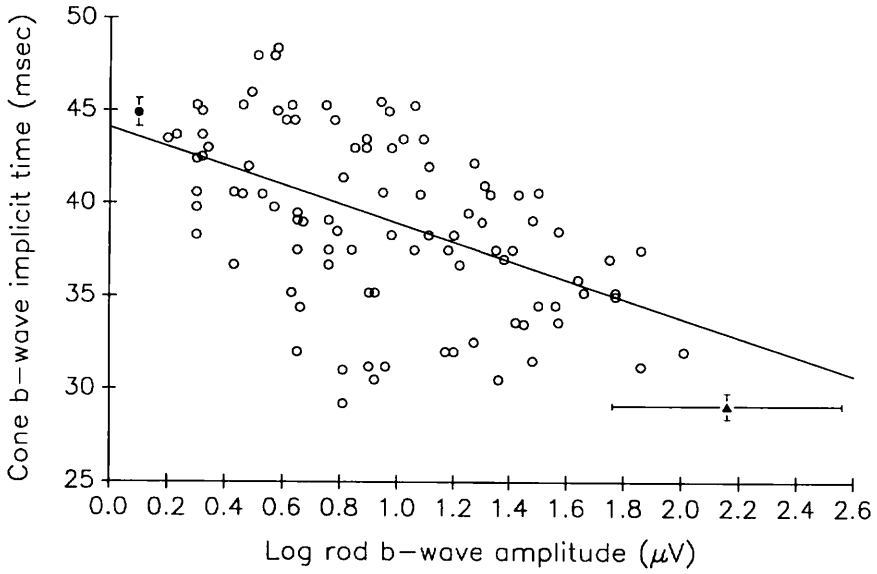

FIG 45–4.
Scatter plot *(open circles)* and linear regression *(solid line)* for cone b-wave implicit time as a function of log b-wave rod amplitude in 100 patients with retinitis pigmentosa and detectable (>1 μV) rod and cone ERGs. Cone ERGs were elicited with 30-Hz white full-field flashes, and rod ERGs were elicited with single-flash short-wavelength flashes. All responses were computer averaged. The regression line ($r = -0.49$; $P < .001$) is $y = 44.2 - 5.3x$. The *solid circle* shows the mean b-wave implicit time (±1 SE) for 109 patients with nondetectable rod responses. The *solid triangle* shows the mean implicit time (±1 SE) for 178 normal subjects.

b-wave implicit time of approximately 4.0 ms over that in the dark (Fig 45–2). The degree to which implicit time decreased was not significantly different between normals and patients (t = .16, NS). Similarly, the steady background decreased the peak-to-peak amplitude by approximately the same percentage in patients and normals. Thus both protocols should be comparably sensitive in detecting an abnormal flicker response. A practical advantage of the lower background level is that it is more likely to yield a detectable response in patients.

The sensitivity of cone b-wave implicit time to retinal degeneration is evident in Figure 45–3. Distributions are shown for 175 normal subjects and 250 patients with retinitis pigmentosa, excluding autosomal dominant individuals, who frequently have normal b-wave implicit times to flicker.[2] Since there is minimal overlap between distributions, 243 of 250 (97%) patients in this sample had significantly (P < .05) delayed cone b-wave implicit times to flicker.

Cone b-wave implicit time is delayed in many young patients at a time when the amplitude may be near normal. While much of the delay is undoubtedly due to intrinsic cone abnormalities, at least part of the delay may result from abnormal rod function. Cone b-wave implicit time in normal subjects varies with the state of rod adaptation.[10] It has been suggested that delayed cone b-wave times in retinitis pigmentosa are due, at least in part, to an absence or functional impairment of rods.[7, 10] As shown in Figure 45–4, there is a significant inverse correlation between cone b-wave implicit time and log rod b-wave amplitude. Among patients with retinitis pigmentosa, the variation in cone loss is not as significant a determinant of cone b-wave implicit time as is the degree of rod loss.[7] These results suggest that progressive rod degeneration leads to the loss of a rod-mediated mechanism that normally acts to shorten cone b-wave implicit time under light adaptation conditions.

REFERENCES

1. Andréasson SOL, Sandberg MA, Berson EL: Narrow-band filtering for monitoring low-amplitude cone electroretinograms in retinitis pigmentosa. *Am J Ophthalmol* 1988; 105:500.
2. Berson EL: Hereditary retinal diseases; classification with the full-field electroretinogram. *Doc Ophthalmol Proc Ser* 1977; 13:149.
3. Berson EL, Gouras P, Gunkel RD, Myrianthropoulis NC: Dominant retinitis pigmentosa with reduced penetrance. *Arch Ophthalmol* 1969; 81:226.
4. Berson EL, Gouras P, Gunkel RD, Myrianthropoulis NC: Rod and cone responses in sex-linked retinitis pigmentosa. *Arch Ophthalmol* 1969; 81:125.
5. Berson EL, Gouras P, Hoff M: Temporal aspects of the electroretinogram. *Arch Ophthalmol* 1969; 81:207.
6. Berson EL, Howard J: Temporal aspects of the electroretinogram in sector retinitis pigmentosa. *Arch Ophthalmol* 1971; 86:653.
7. Birch DG, Sandberg MA: Dependence of cone b-wave implicit time on rod amplitude in retinitis pigmentosa. *Vision Res* 1987; 27:1105.
8. Gouras P, Mackay CJ, Ivert L, Mittl RN, Neuwirth J, Eggars H : Computer-assisted spectral electroretinography in vitrectomy patients. *Ophthalmol* 1985; 92:83.
9. Hecht S, Schlaer S: Intermittent stimulation by light. V. The relation between intensity and critical frequency for different parts of the spectrum. *J Gen Physiol* 1936; 19:965.
10. Sandberg MA, Berson EL, Effron MH: Rod-cone interactions in the distal human retina. *Science* 1981; 212:829.