BASIC PRINCIPLES OF CLINICAL ELECTRORETINOGRAPHY

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Abstract: Before applying the technique of electroretinography to the investigation of retinal disorders, it is imperative to understand the cells within the retina that generate its component waveforms and the manner in which various stimuli and background conditions modify their amplitude and isolate cone and rod contributions. RETINA 5:123–126, 1985

The full-field, light-elicited electroretinogram (ERG) records a diffuse electrical response developed by cells within the retina. This response, representing the algebraic summation of several component waves, occurs as the result of light-induced changes in the transretinal movements of sodium and potassium ions in the extracellular space. Dewar, in 1877, first recorded this electrical response in humans. The majority of investigations was limited to animals until 1941, when Riggs developed a recording electrode that was practical for human use.

The absorption of light by visual pigment within photoreceptor outer segments initiates a sequence of not yet fully understood molecular events localized to these segments that generates (in vertebrate retinas) a wave of hyperpolarization of the photoreceptors. This hyperpolarization (negative change in intracellular electrical potential) results from a light-induced decrease of the inward-directed sodium current across the plasma membrane of photoreceptor outer segments (more precisely, a decrease in sodium conductance of the plasma membrane). The electrical change thus generated can be measured clinically as the corneal negative a-wave of the ERG.

The light-induced hyperpolarization of the photoreceptor diminishes the release of a neurotransmitter at the synaptic terminals of the photoreceptors. This modulation of neurotransmitter release in turn causes a depolarization or hyperpolarization at the postsynaptic bipolar and horizontal cells. Subsequently, arising changes in extracellular potassium, primarily within postreceptor layers, are sensed by Mueller (glial) cells. The resulting electrical response of the Muller cells is the primary generator of the corneal positive b-wave of the clinical ERG. If only a- and b-wave components are considered, the ERG is completed in less than 1/4 second.

Changes in extracellular potassium also alter a standing potential at the level of the retinal pigment epithelial cells. Subsequent to a flash of light, a transient alteration of this potential and electrical changes within the Muller cells induces a monophasic, corneal positive deflection that follows the b-wave, referred to as the c-wave of the ERG. Electrical events within ganglion cells or optic nerve fibers do not generate the ERG a- or b-waves. Thus disorders of the
retina, such as glaucoma and various types of optic atrophy, that selectively affect ganglion cells and/or optic nerve axons do not ordinarily reduce ERG a-wave or b-wave amplitudes. Since the ERG b-wave is dependent on electrochemical events that generate the ERG a-wave, any retinal disorder that prevents the generation of a normal a-wave will also affect the development of a normal ERG b-wave. Examples include retinitis pigmentosa, retinal detachment, and ophthalmic artery occlusion.

The converse, however, is not true. Disorders that result in a diffuse degeneration of cells within the inner nuclear layer (Muller cells and bipolar cells) can selectively decrease the ERG b-wave without diminishing the ERG a-wave. A notable example is in central retinal artery occlusion. To reduce a- and/or b-wave amplitudes, a disorder must have a diffuse effect on retinal tissue. Thus focal lesions of the fovea (defined as a region the approximate size of the optic disc, 1.5 mm in diameter, centered at the foveola) do not affect the a- and b-wave amplitudes elicited by a full-field flash stimulus. The work of Armington and co-workers suggests that a loss of one half of the photoreceptors across the entire retina may result in approximately a 50% reduction in ERG amplitude. Although results vary, the authors of one study of 11 diabetic patients noted that panretinal photocoagulation reduced a- and b-wave amplitudes from pretreatment recordings by approximately 50%.

Factors other than retinal cell degeneration, for example various anesthetics, alter ERG a- and b-wave amplitudes. Thus caution is warranted not to misinterpret reductions in ERG waveform amplitudes unless the potential role of an anesthetic can be ascertained. Further, caution is warranted when interpreting ERG recordings from infants who may not show adult amplitude levels until 1 year of age.

Diffuse degeneration or a malfunction of retinal pigment epithelial cells reduces the c-wave amplitude of the ERG. Special recording electrodes, DC amplification (unlike AC amplification used for standard ERG recordings), and bright-light stimuli are necessary for an optimal recording of the ERG c-wave. These procedural constraints, in addition to the wide physiologic variability in c-wave amplitude, have limited the clinical application of c-wave measurements.

In addition to measurements of a- and b-wave amplitudes, clinical ERG studies can quantitate small amplitude oscillations that occur on the ascending limb of the ERG b-wave, referred to as oscillatory potentials. These waves appear to derive primarily from activity of the amacrine cells. Their amplitudes are negatively affected by diffuse ischemic disorders of the inner retina such as diabetic retinopathy or retinal vascular occlusion.

Stimulus Conditions

In addition to light stimuli, patterns such as a checkerboard or sinusoidal grating can be used to elicit an ERG response. The resultant recordings are being investigated to monitor, among other variables, the effect different contrasts of the stimulus have on the resultant waveforms. Depending on the size of the checkerboard pattern and contrast levels, the pattern ERG waveforms currently are thought to originate from within retinal ganglion cells.

Besides full-field flash ERG recordings, focal light stimuli can be used to stimulate the fovea selectively. This technique is somewhat demanding for both stimulus and recording conditions of the small amplitude responses and thus is not used routinely in clinical testing. A signal averager, with an artifact rejection function, and control of stimulus stray light are mandatory to record a focal ERG from the fovea.

An important element in full-field flash ERG measurements relates to characteristics of the light stimulus employed. With weak or moderately intense light stimuli, the ERG a-wave is either not apparent or substantially less apparent than the b-wave. It takes approximately 1 log unit more of light to detect an a-wave after the b-wave first becomes apparent. Figure 1 shows ERG a- and b-waves with different

![Fig. 1. The effect of various intensity white flash stimuli on the ERG amplitude, waveform, and implicit time.](image)
light intensities. Not unexpectedly, brighter light stimuli produce larger a- and b-wave amplitudes. Further, brighter stimuli elicit a proportionately greater a-wave contribution to the ERG and shorter a- and b-wave implicit times (i.e., the period from stimulus onset to the peak of the respective component of the response). Dense media opacification, such as vitreous hemorrhage or marked cataractous lens changes, can reduce the ERG a- and b-wave amplitudes and prolong their implicit times.

In addition to intensity, the color of the light stimulus influences the ERG waveform (Fig. 2). A low-intensity blue stimulus elicits an ERG that is predominantly b-wave and essentially consists of only a rod contribution. The use of a red stimulus shows a response with two distinct positive peaks. The first, referred to as the x-wave of Motokawa and Mita, is a cone component; the second positive peak (b-wave) results from rod activity. In addition to intensity and color, the stimulus rate can be varied. Since rods cannot respond to flickering stimuli above approximately 15 cycles per second (cps), a stimulus flickering at 30 cps elicits a pure cone response.

**Isolation of Cone and Rod Responses: Recording Techniques**

The ultimate purpose of a clinical flash ERG is to determine the overall functional integrity of retinal cones and rods. It is necessary, therefore, to implement recording techniques that selectively isolate cone and rod contributions to the ERG. The measurement of either component is determined by the physiology of the retina and its response to light stimuli of various intensities, color, and rates. A recording contact lens with a conductive material component can serve as an active electrode to detect differences in electrical potentials between the retina and cornea and to transmit these electrical signals for amplification and subsequent display.

In the clinical ERG setting, a reference or neutral electrode obviously cannot be placed in direct contact with the retina. Fortunately, electrical potential differences between the retina and cornea that occur subsequent to a flash of light can be detected by a metallic reference electrode placed in the periorcular region. This electrode is usually applied to the forehead with electrode paste. A ground electrode is commonly applied to the earlobe. If a bipolar recording contact lens is used, a reference electrode is incorporated as part of the lid speculum, obviating the need for a separately placed skin reference electrode.

Once all electrical contacts are made between the cornea and periorcular tissues, cone function can be isolated by exposing the retina to a background light, which is most effectively generated within a diffusing sphere. A diffusing sphere allows for more even illumination of the retina by both the background light and the stimulus and provides a more homogeneous response from retinal elements. Since the background light produces a suppression of rod function by a mechanism other than the bleaching of an appreciable amount of visual pigment, the background light can be relatively dim (range, 7–10 ft-lamberts). If the background light is very dim or not diffusely illuminating the retina, the response under “photopic” conditions can contain a rod contribution. If the background light is too intense, the cone response will be suppressed to an appreciable degree. Thus, in addition to disorders of the retinal cells and characteristics of the stimulus, the background intensity on which the stimulus is superimposed can influence retinal adaptation and therefore the ERG amplitude and its cone-versus-rod contributions.

The photopic ERG has both a- and b-wave components. In humans, the photopically (light-adapted) obtained ERG results from sampling approximately 6–8 million cones; the a- and b-wave responses (compared with scotopic responses) are small. The b-wave is in the range of 110–150 μV, depending on the stimulus intensity, background illumination, type and size of diffusing sphere, etc. (Fig. 3). Cone function also is isolated by using a flash stimulus flickering faster than 20 cps. Most laboratories use a flickering rate of 30 cps (Fig. 2).

Rods can be isolated by dark-adapting the retina and using the appropriate stimulus. An adaptation period of at least 30 minutes is necessary to determine the maximal response under scotopic (dark-adapted)
Fig. 3. ERG recordings taken with high-intensity white flash stimuli under light adaptation and various periods of dark adaptation.

conditions. Although opinions vary, the terms "photopic" and "scotopic" should probably refer to the state of retinal adaptation and not imply selective cone or rod function. Although under a photopic state of adaptation the ERG response subsequent to a light stimulus is essentially a pure cone response, an ERG obtained under scotopic conditions with a bright white light stimulus is not a pure rod response. In fact, even though obtained under scotopic conditions, the stimulation by a bright flash elicits a- and b-wave components of both cone and rod pathways. These responses are algebraically summed by the recording equipment and are displayed as a combined cone and rod response (Fig. 3). In normal subjects, the predominant contribution to this combined response is clearly from the rod system, probably because the rod-to-cone ratio is approximately 17:1. However, when small responses are obtained with bright white stimuli under scotopic conditions from a diseased retina, the scotopic response may have a substantial cone contribution if rods are appreciably more affected by the disease process than are the cones. Rod responses can be isolated by using a low-intensity and preferably blue flash stimulus. This stimulus can be flickered at 10 cps to examine rod responses in a sinusoidal waveform (Fig. 2). Both cone and rod components can be assessed with a single red flash stimulus under scotopic conditions. The initial positive deflection (x-wave) is a cone component and the subsequent positive peak (b-wave) is a rod component (Fig. 2).

When apparent in the recording from brighter light stimuli, the a-wave is measured from the baseline to the lowest point (trough) of the negative deflection. The b-wave is traditionally measured either from the baseline, when no a-wave is present, or from the trough of the a-wave to the peak of the positive deflection. In addition to a- and b-wave amplitudes under photopic and scotopic conditions, values for their implicit times are determined. The ERG implicit time may be altered (prolonged) by diffuse photoreceptor diseases, such as retinitis pigmentosa. However, stimulus and background conditions can alter implicit times. Brighter backgrounds and brighter stimuli promote shorter implicit times (Fig. 1).

Because the ERG varies with different stimulus conditions and physiologic features, such as the type of ganzfeld (diffuse homogeneous retinal stimulus) apparatus used, each laboratory must carefully establish its own set of normal values for cone and rod amplitudes and implicit times. Age, sex, and refractive error (high myopia) should be considered when evaluating normal versus abnormal responses. Since normal ERG amplitude responses tend not to have a Gaussian distribution, nonparametric statistical techniques may need to be employed.

Facility with the technology for recording ERGs is only the initial step toward implementation that is meaningful. When to apply and when not to apply ERG testing to patients suspected of having various retinal disorders is necessary as well.

Subsequent reviews will examine the application of ERG technology to various retinal disorders.

**Key words:** electroretinogram, photopic, scotopic, hyperpolarization, potassium.

**References**


