

ELECTRORETINOGRAM (ERG)

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1. Core Definition

The **Electroretinogram (ERG)** is a crucial electrophysiological test used to record the electrical responses generated by various cells in the retina when stimulated by light. This diagnostic tool provides an objective measure of the functional integrity of the photoreceptors (rods and cones), bipolar cells, Müller cells, and other inner retinal neurons. The ERG captures massed electrical potentials resulting from the photochemical and subsequent neurophysiological processes initiated when light strikes the eye. Unlike subjective visual acuity tests, the ERG offers a quantitative assessment of retinal health, making it indispensable in diagnosing inherited and acquired retinal diseases.

The recording process typically involves placing an electrode (often a corneal contact lens electrode or a small fiber electrode) directly on the cornea, while a reference electrode is placed on the surrounding skin (e.g., the forehead or temple). A ground electrode completes the circuit. When a standardized light stimulus (a flash or a patterned display) is presented, the resulting small electrical potential difference between the active and reference electrodes is amplified and recorded. This resulting waveform, the ERG, represents the time-locked summation of cellular activities within the retina, reflecting the health and sensitivity of the different retinal layers.

Crucially, the ERG is a measure of the retina's overall electrical output and should not be confused with other ocular electrophysiological tests, such as the Electrooculogram (EOG) or the Visual Evoked Potential (VEP). While the VEP measures the response of the visual cortex to visual stimuli, the ERG specifically isolates the activity occurring within the retinal layers themselves. This isolation allows clinicians to pinpoint the anatomical location of a visual processing defect, determining whether the pathology lies in the primary light-sensing structures or further along the visual pathway.

2. Etymology and Historical Development

The term **Electroretinogram** is derived from Greek roots: *elektron* (related to electricity), *retina* (referring to the light-sensitive tissue), and *gramma* (meaning writing or recording). The earliest foundational work leading to the ERG was conducted in 1865 by the Swedish physiologist Alarik Frithiof Holmgren, who first recorded electrical activity from the frog retina in response to light. This initial discovery established the physiological basis that the retina produces measurable electrical signals upon photic stimulation, demonstrating that the visual process is inherently tied to electrical changes.

Significant progress followed in the early 20th century, particularly with the work of German researchers who refined the techniques. However, it was the clinical application and standardization developed by researchers in the mid-20th century that truly cemented the ERG's role as a diagnostic tool. Key developments included the use of corneal contact lens electrodes, which allowed for non-invasive testing in humans, and the refinement of amplification equipment necessary to capture the microvolt-level potentials. These advancements led to the standardization protocols established by the International Society for Clinical Electrophysiology of Vision (ISCEV), ensuring that ERG recordings are comparable across different clinical settings globally.

Initially, ERGs were simple flash recordings, providing a general assessment of mass retinal function. The subsequent development of specialized techniques, such as the pattern ERG (PERG) and the multifocal ERG (mfERG), allowed for the isolation of specific cell types (e.g., ganglion cells) and mapping of localized retinal areas, respectively. This evolution has transformed the ERG from a crude measure of overall health into a highly nuanced diagnostic instrument capable of revealing subtle, localized pathology, greatly enhancing the ability to diagnose complex conditions like glaucoma and macular degeneration early.

3. Key Wave Components

The standard full-field flash ERG waveform is characterized by three primary components, or waves, each corresponding to the electrical activity of different retinal cell layers. Analyzing the amplitude and timing (latency) of these waves provides critical diagnostic information about the locus of retinal dysfunction.

The initial negative deflection is termed the **A-wave**. This wave primarily reflects the activity of the outer retina, specifically the hyperpolarization of the photoreceptor cells (rods and cones) in response to light absorption and the resultant drop in the dark current. The peak amplitude of the A-wave is measured from the baseline to the deepest negative point, and its latency reflects the speed of phototransduction. A reduced A-wave amplitude suggests damage or dysfunction primarily located in the photoreceptor layer, often seen in conditions like retinitis pigmentosa where the primary sensory cells are degenerating.

Following the A-wave is the positive deflection known as the **B-wave**. This is typically the largest component of the ERG and reflects the activity of the inner retinal layers, specifically the depolarizing activity of the bipolar cells and Müller cells. The B-wave amplitude is measured from the trough of the A-wave to the peak of the B-wave. Dysfunction in the inner nuclear layer, such as in certain forms of stationary night blindness, disproportionately affects the B-wave relative to the A-wave, leading to a phenomenon known as an electronegative ERG, where the negative A-wave dominates the trace.

A third, much slower component, the **C-wave**, represents the activity of the retinal pigment

epithelium (RPE) and is often less commonly used in standard clinical settings due to its slow nature and technical difficulty in reliable recording. Furthermore, smaller, high-frequency oscillations known as **Oscillatory Potentials (OPs)** ride on the rising phase of the B-wave. These OPs are thought to originate from amacrine cells and are particularly sensitive indicators of retinal ischemia (lack of blood flow), making them valuable in monitoring conditions that affect retinal circulation, such as severe diabetic retinopathy.

4. Key Recording Modalities and Techniques

Clinical practice utilizes several variations of the ERG, each tailored to isolate specific retinal functions or localized areas, ensuring a comprehensive evaluation of the visual system. These variations adhere to strict ISCEV protocols to ensure reliable interpretation.

Full-Field (Ganzfeld) ERG: This is the fundamental test, recorded using a dome or sphere (Ganzfeld) that provides uniform, diffuse illumination across the entire retina. It yields a mass response, representing the summed activity of nearly all rods and cones and subsequent inner retinal cells. Protocols mandate specific light intensities and adaptation states--dark adaptation for assessing rod function (scotopic conditions) and light adaptation for assessing cone function (photopic conditions)--to differentiate between the two primary sensory systems.

Pattern ERG (PERG): The stimulus here is a structured pattern, typically an alternating checkerboard or grating display, rather than a diffuse flash. The PERG is generated primarily by the activity of retinal ganglion cells and their post-receptoral input, making it uniquely sensitive to diseases affecting the innermost retina and the optic nerve, such as **glaucoma**. A reduced PERG with a normal full-field ERG strongly suggests a functional problem originating at the ganglion cell layer or optic nerve head, indicating selective inner retinal damage.

Multifocal ERG (mfERG): Developed to overcome the limitation of the full-field ERG--its inability to assess localized damage--the mfERG uses a complex array of many small, flickering hexagonal stimuli presented simultaneously. This technique allows for the generation of hundreds of miniature ERG responses corresponding to specific areas of the retina, providing a detailed functional map of the central and mid-peripheral macula. It is invaluable for tracking the progression of focal macular diseases, such as age-related macular degeneration or toxic maculopathy.

Photopic Negative Response (PhNR): A specific negative component of the photopic (cone-driven) ERG that follows the B-wave. The PhNR is thought to originate primarily from the retinal ganglion cells and is a robust biomarker for monitoring the early stages of glaucoma and other optic neuropathies. Changes in the PhNR often precede measurable structural damage to the optic nerve head.

The selection of the appropriate ERG modality is critical and guided by the suspected etiology. For example, hereditary retinal dystrophies often require a full-field ERG under both scotopic and photopic conditions for grading severity, while localized optic nerve diseases require the sensitivity

of the PERG and PhNR assessment.

5. Clinical Significance and Applications

The ERG is an essential tool in clinical diagnostics, offering objective evidence of retinal function that cannot be obtained solely through imaging or subjective testing. It is particularly crucial when the clinician suspects a hereditary retinal disorder, or when opaque media (like dense cataracts or vitreous hemorrhage) prevent visual examination of the posterior pole of the eye, providing the only functional assessment available.

Major applications include the diagnosis and monitoring of numerous congenital and acquired disorders. Inherited conditions such as **Retinitis Pigmentosa (RP)** typically show progressive loss of both rod and cone ERG amplitudes, reflecting widespread photoreceptor degeneration. In contrast, congenital stationary night blindness (CSNB) may present with characteristic waveform abnormalities, such as an electronegative ERG, indicating a specific failure in signal transmission between photoreceptors and bipolar cells while the photoreceptors themselves remain healthy, allowing for differentiation between these clinically similar presentations.

Beyond hereditary diseases, the ERG is vital in assessing toxic retinopathies caused by certain systemic medications (e.g., hydroxychloroquine or vigabatrin), providing an early warning sign of drug-induced retinal damage before irreversible vision loss occurs. It is also used to determine retinal viability in eyes undergoing complex surgery, assess retinal damage following trauma or retinal detachment, and monitor the progression of vascular diseases like central retinal artery or vein occlusion. The objective nature of the ERG ensures that retinal function can be quantified and tracked over time, providing invaluable data for longitudinal studies and clinical trials assessing novel treatments.

6. Debates and Criticisms

While the ERG is highly valued for its objectivity, it faces several inherent technical and interpretive limitations. A significant challenge relates to the fact that the full-field ERG is a **mass response**, meaning it averages the activity of the entire retina. Consequently, it is insensitive to focal, subtle damage if the surrounding retinal area remains healthy. For example, a small, central scotoma caused by early macular disease might not significantly alter the overall full-field response because the vast, healthy peripheral retina masks the defect. This limitation necessitates the reliance on specialized techniques like the mfERG to detect localized pathology, adding complexity and time to the testing protocol.

Interpretation also presents challenges due to the high degree of standardization required. The results are highly dependent on the patient's state of adaptation (e.g., ensuring complete dark adaptation before scotopic testing), pupil size, media clarity, and fixation stability, especially for

localized tests. Artifacts caused by patient movement, blinking, or electrical interference can contaminate the recording, requiring experienced technicians and specialized signal processing to ensure data quality. Furthermore, while the ERG accurately measures electrical function, it does not provide anatomical detail; therefore, it must always be interpreted in conjunction with structural imaging tests like Optical Coherence Tomography (OCT) to correlate functional loss with physical damage.

There is also ongoing debate regarding the exact cellular origins of some smaller components, such as the oscillatory potentials, and how precisely these correlate with specific pathogenic processes like early diabetes. Continuing research aims to enhance the specificity of ERG techniques, possibly through adaptive optics or higher-density electrode arrays, to provide even finer detail about individual cell layer activities, moving beyond the traditional A- and B-wave analysis to offer a more precise cellular diagnosis.

7. Further Reading

[Electroretinography \(Wikipedia\)](#)

[International Society for Clinical Electrophysiology of Vision \(ISCEV\)](#)

[American Academy of Ophthalmology \(AAO\) on ERG](#)