Electrophysiology in Retinitis Pigmentosa

By

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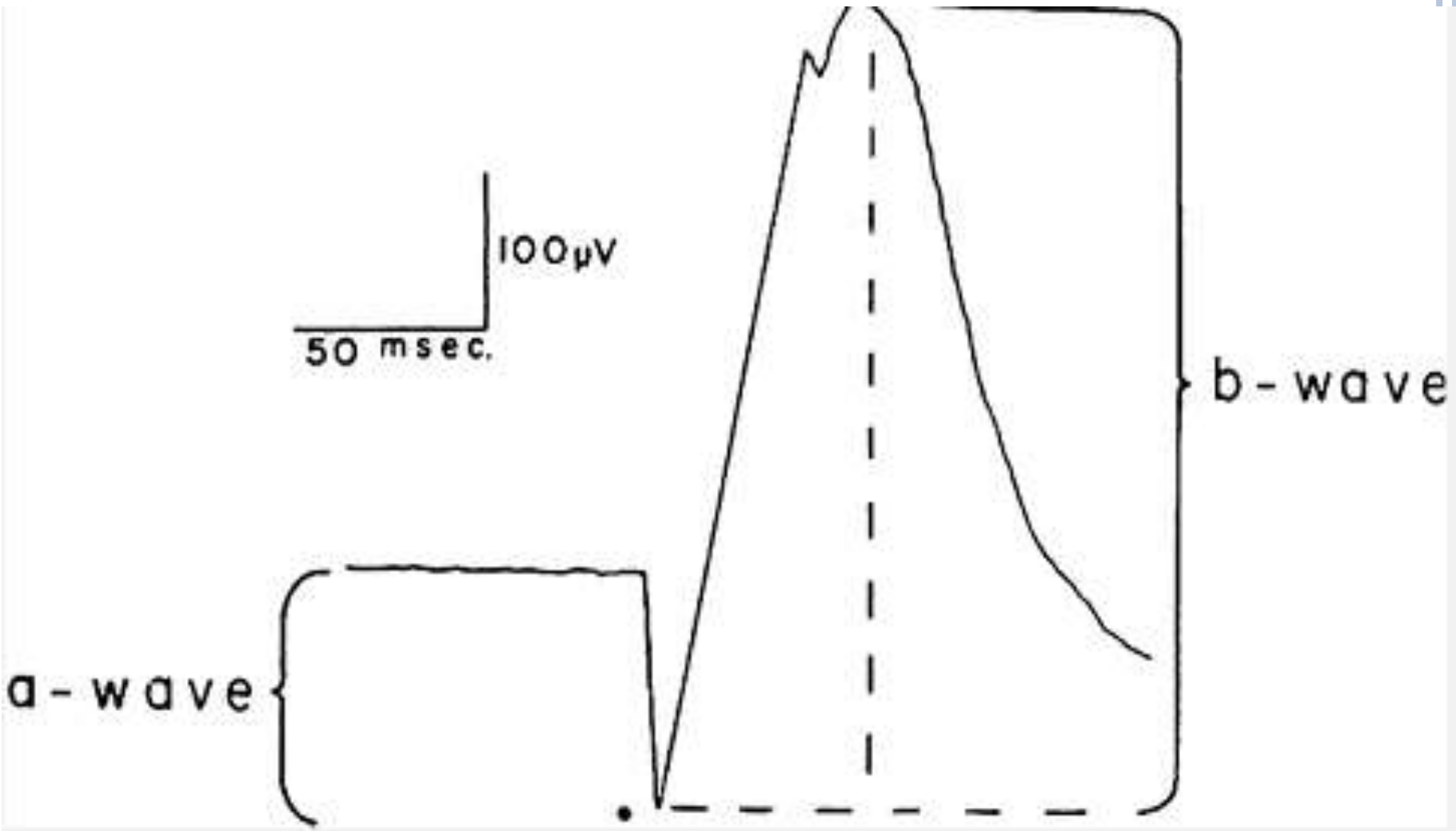
ERG

(ELECTRORETINOGRAM)

INTRODUCTION

- So simply, it is the light evoked electrical response of the retina .
- The response occurs as a result of transient movements of ions in the extracellular space induced by the light stimulus.
- In the clinical setting, only the early electrical responses of the retina (within the initial 200 msec) are measured, because later responses usually are obliterated by eye blinks. Within this 200 msec time frame, two predominant responses occur: the a-wave and the b-wave .

ERG Response



- The **a-wave** is the initial downgoing deflection, and it arises from the photoreceptor cells. The **b-wave** is the upgoing deflection that follows the a-wave, and it arises from the Muller cells. Although the derivation of the b-wave is from Muller cells, it reflects such activity from the region of the bipolar cells.
- Under certain recording conditions, small wavelets, called oscillations, may be seen riding on the downgoing and upgoing waves. These oscillatory potentials arise from a number of cell types in the midretinal layers.
- it is clear that the ganglion cells play no role in the generation of the ERG. Therefore, diseases affecting only the inner retina or the optic nerve should not alter the ERG.

Stimulus Condition

- **Aim:** isolation of either the cone or rod responses, so that each receptor can be studied independently.
- **Standardized Protocol:**

1- A maximal response in the dark-adapted eye

2- A response developed by the rods (in the dark-adapted eye)

3- Oscillatory potentials

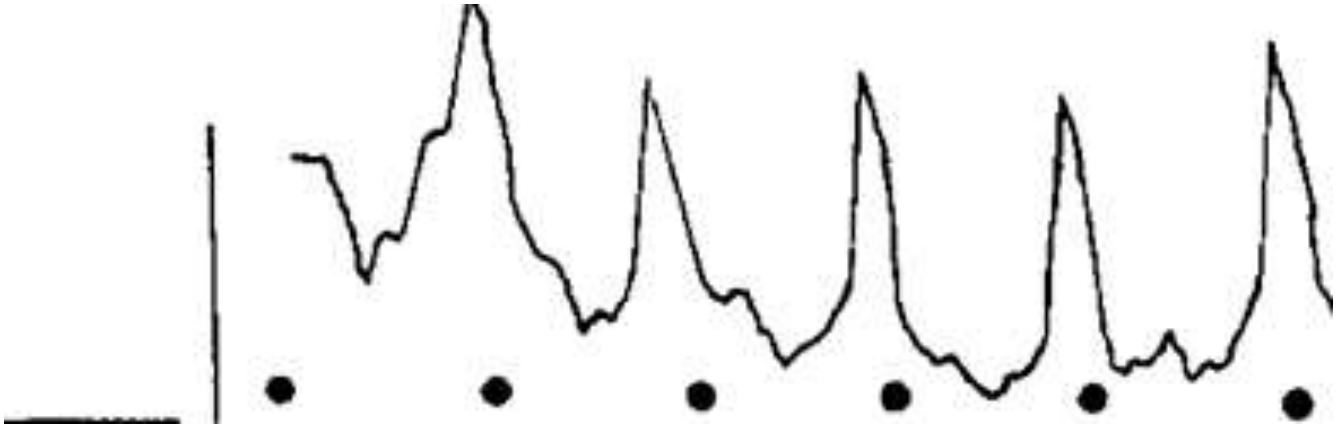
4- A response developed by the cone

5- Responses obtained to a rapidly repeated stimulus (flicker)

(International Standardization Committee)

Cone Response

- Under photopic or light-adapted conditions with a bright background light, the rods are sufficiently dampened so that the only response is from the cones.
- The cone response is rapid, with a b-wave implicit time usually between 28 and 32 msec.
- The cone response also can be isolated by using a rapidly flickering light. The cones follow a flickering light of up to 60 to 70 Hz, whereas the rods follow a flickering light only up to 12 to 16 Hz. Therefore, a stimulus flickered at 30 Hz elicits a response only from the cone receptors



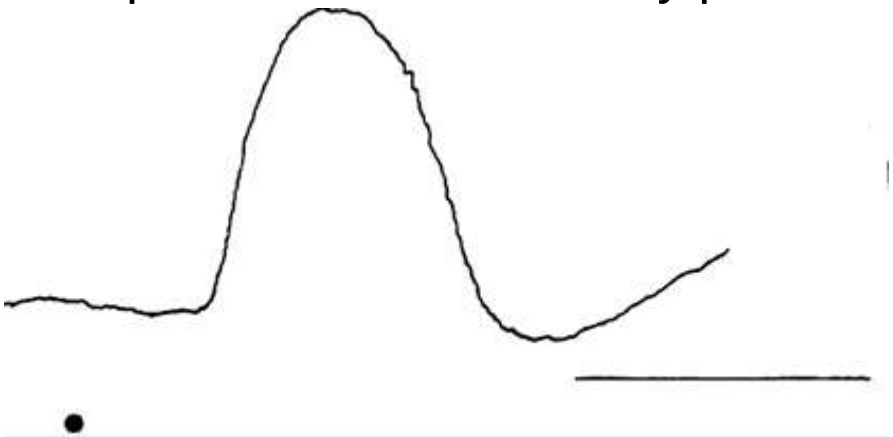
Flicker ERG. A repetitive high-intensity flash (30/sec) produces this all-cone response

ROD RESPONSE

After sufficient dark adaptation (30 min), the rod responses are optimized under these scotopic conditions.

A single bright flash gives a response that is a composite of the dark-adapted rods and the dark-adapted cones. This response is much larger and has a longer implicit time than is the pure cone response.

How, then, does one look at the rods alone? Because the rods are very sensitive to light at the blue end of the spectrum, a weak blue-light stimulus produces an essentially pure rod response

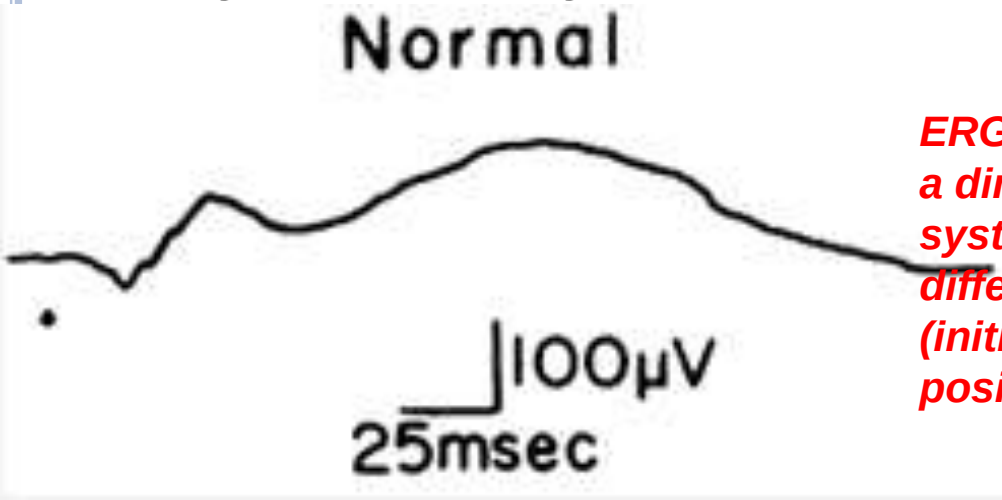


ERG response of the dark-adapted eye to a dim blue flash

Biphasic Response

(A maximal response in the dark-adapted eye)

A red stimulus under scotopic conditions results in a biphasic response in which the initial wave represents the more rapidly responding cones and the second response the slower responding rods. This biphasic response occurs because the rods are relatively insensitive to light at this longer wavelength.



ERG response of the dark-adapted eye to a dim red flash. Left: Rod and cone systems respond with sufficient difference to allow separation of cone (initial positive response) and rod (second positive response) systems

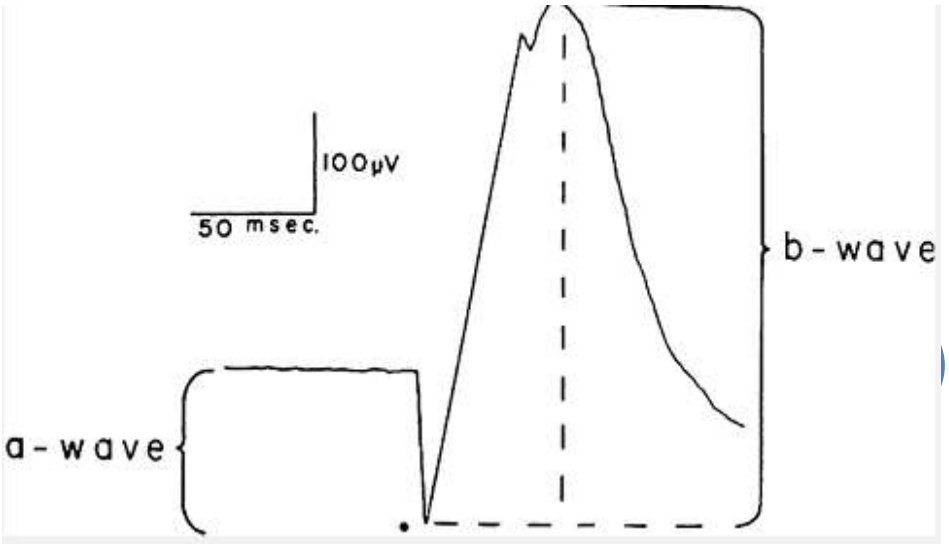
Oscillatory Potentials

- Valuable in assessment of mid retinal layers.

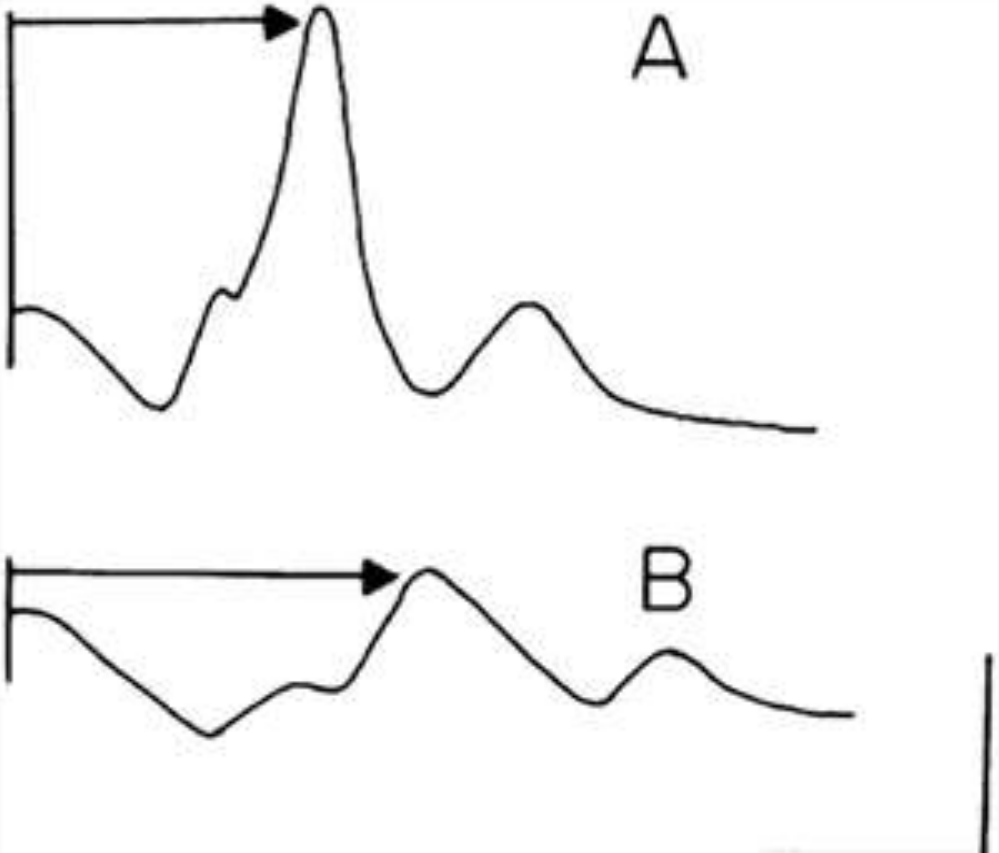
Left: Dark-adapted ERG demonstrating the oscillatory potentials riding the ascending limb of the b-wave. Right: By selective filtering, the slower components of the ERG, including the b-wave, can be eliminated, leaving only the fast-frequency components, the a-wave, and the oscillatory potentials

PARAMETERS

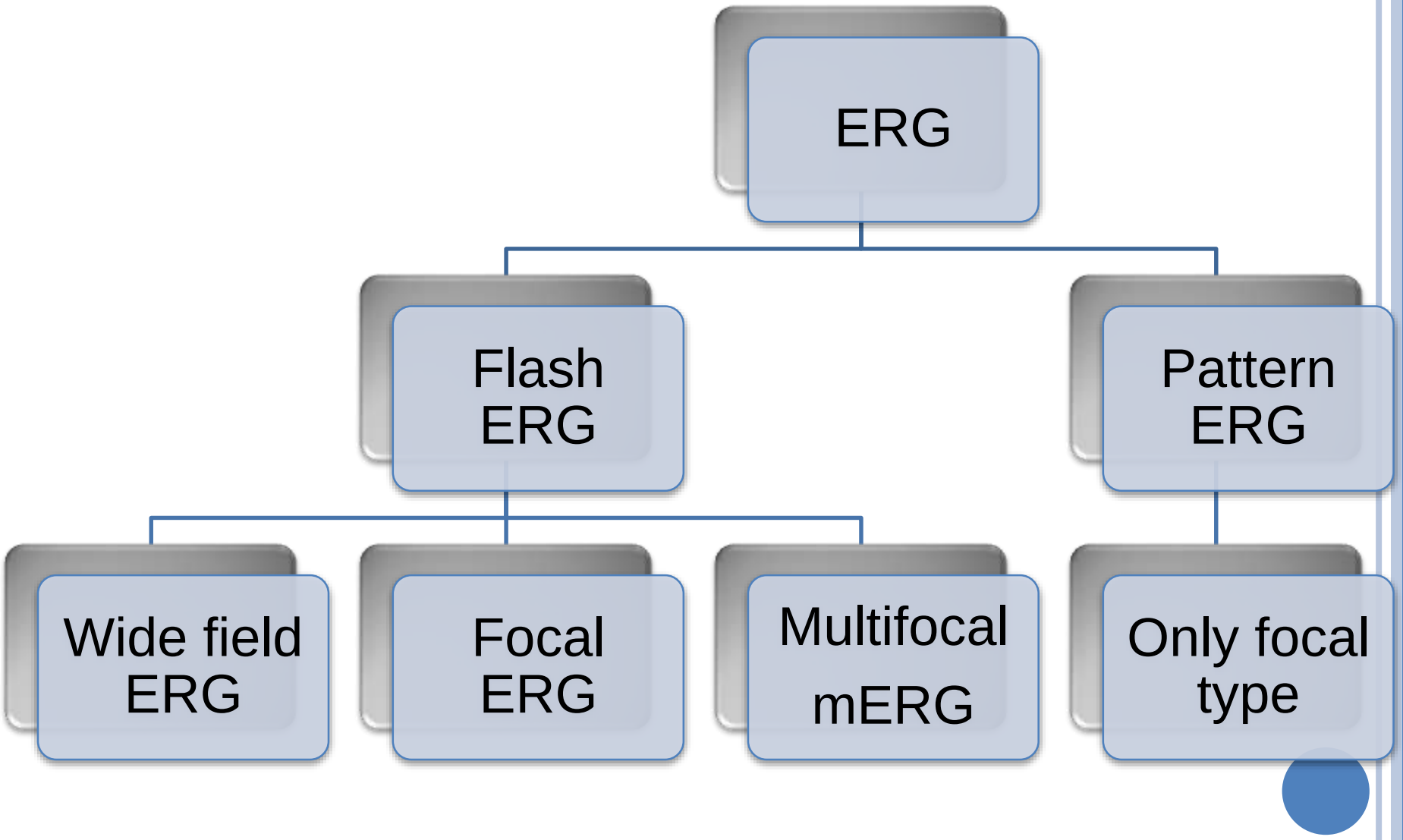
- Two major parameters are used to evaluate the ERG response in the clinical setting !
- The first is the **amplitude** of the wave, which is measured in microvolts (μV). The amplitude of the a-wave is measured from the baseline to the trough of the a-wave, whereas the b-wave is measured from the trough of the a-wave to the peak of the b-wave.



- The **implicit time** is the second major parameter. It is defined as the time from the stimulus onset to the peak of the response and is measured in milliseconds.
- The easiest and most accurate measure of the implicit time is the b-wave under light-adapted or photopic conditions .



The implicit time is measured from the stimulus to the peak of the response. A:. Normal. B: Patient with retinitis pigmentosa showing a reduced amplitude b-wave with an increased implicit time.


ERG
Flash ERG
Pattern ERG
Wide field ERG
Focal ERG
Multifocal mERG
Only focal type

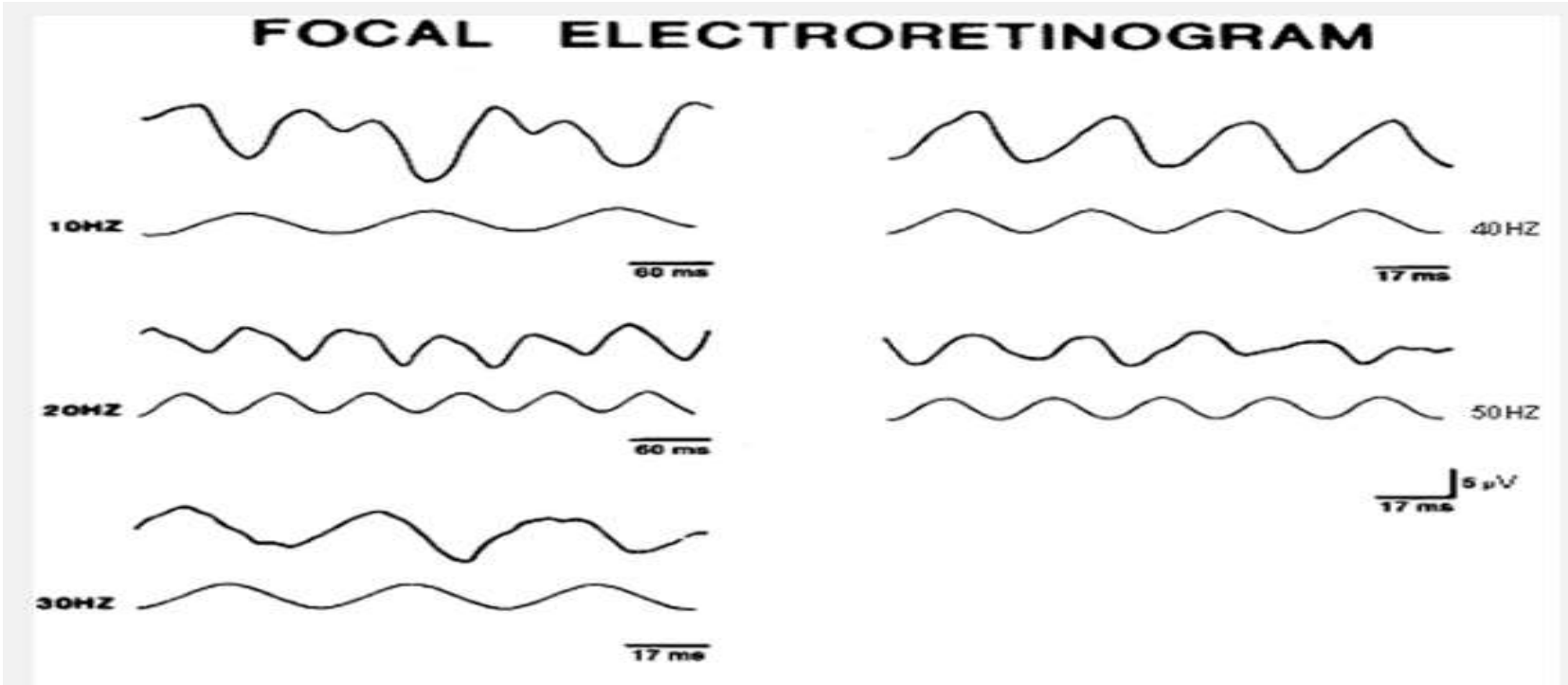
Wide Field ERG

- It is a mass response generated by cells across the entire retina.
- Although the rods outnumber the cones 13 to 1, the cones account for 20% to 25% of the full-field ERG response to single flashes of white light under dark-adapted conditions.
- The full-field ERG is primarily generated by extramacular (i.e., midperipheral and far peripheral) cones and rods, because patients with a four-disc diameter central scar and normal extramacular function have normal full-field cone and rod ERG responses.

FOCAL ERG

- Can be Flash ERG or Pattern ERG.
- Can visualize stimuli on the fundus and record from focal areas within the macula. These focal ERGs are elicited with a stimulator ophthalmoscope.
- With this instrument, a 4-degree, 42-Hz white flickering stimulus is presented within a 10-degree white steady surround; this flickering stimulus allows isolation of cone function, and the steady surround permits visualization of the fundus. The surround also desensitizes the retina just outside the stimulus, thereby minimizing any possible responses that could be generated by the effect of stray light from the stimulus.

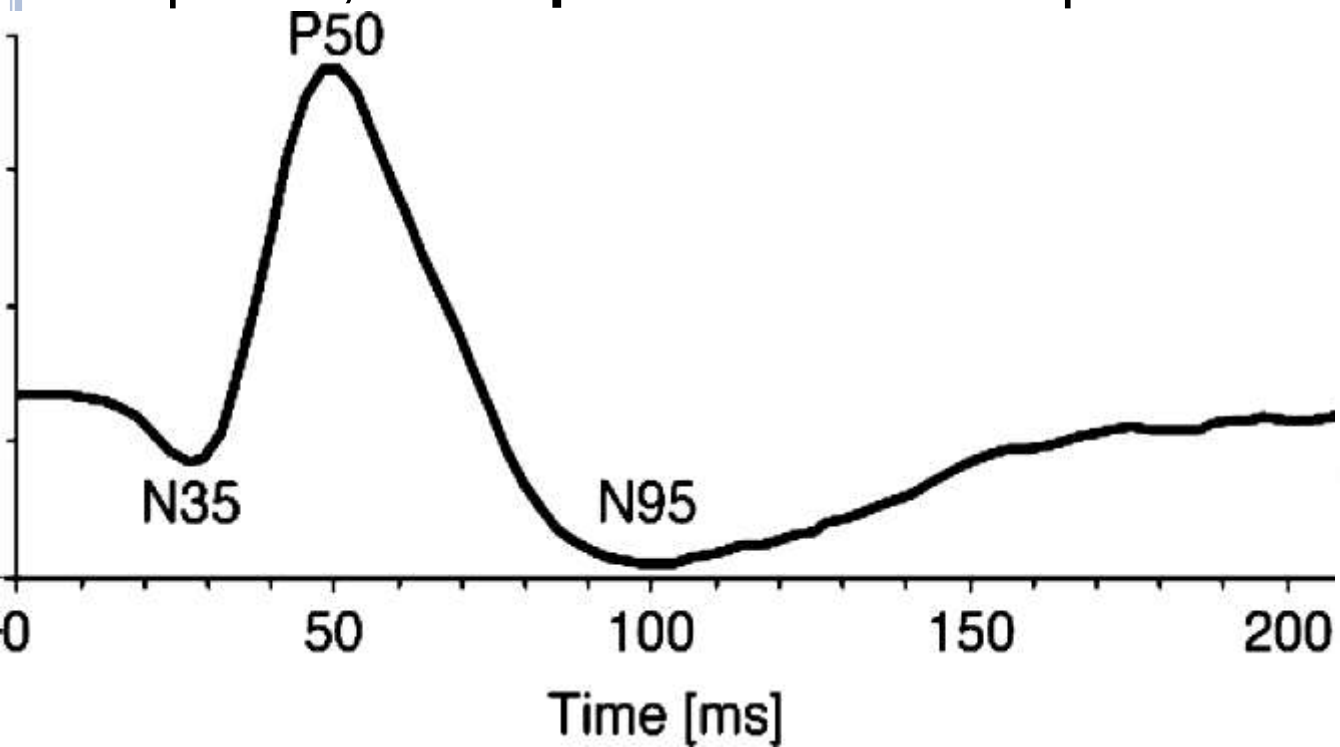
- A normal FERG, as recorded over a range of frequencies, has its peak at a frequency between 30 Hz and 40 Hz . Likewise, the latency of the FERG response (phase lag) varies with frequency.
- Using these two parameters, amplitude and latency, helps to diagnose a patient with early macular degeneration or conversely, to demonstrate normalcy of the central cone system in a patient with reduced vision.



PATTERN ERG (PERG)

- Responses from the central retina can be elicited not only in response to flashes of light, but also in response to a phase reversing pattern stimulus, usually a grating or checkerboard displayed on a television screen.
- The pattern elements (checks or bars) periodically reverse position, so that the bright bars become dim and vice versa, although the sum of all bars has a constant brightness at all times.
- The clinical value of the pattern electroretinogram (PERG) for diagnoses (ganglion cells), as well as following the course of certain diseases, has been studied in ocular hypertension, glaucoma, optic neuritis, optic atrophy, and amblyopia.

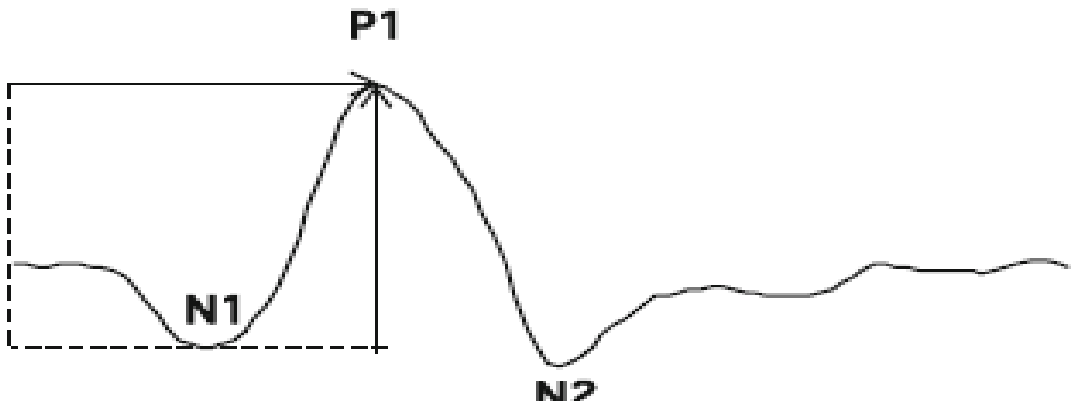
- A typical standard PERG. The amplitude of the P50 is typically between 2.0 and 8.0 uV
- The term **“latency”** is commonly misused when referring to the peak time or implicit time. Latency should be used to refer to the time to the onset of a response, not to the peak of the response; thus **“peak time”** is the preferred term.

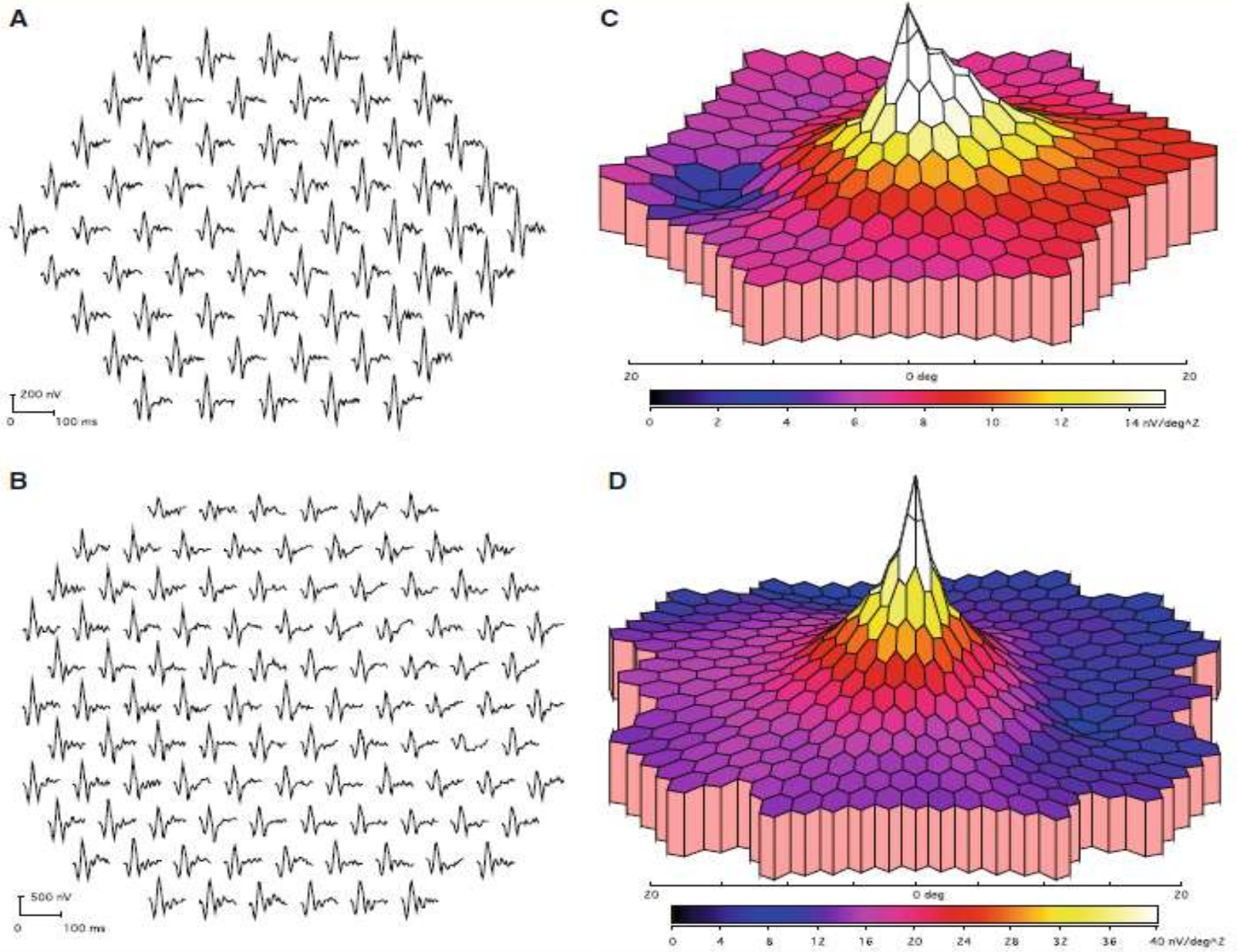


MULTIFOCAL ERG (MERG)

- multifocal ERG system in which multiple retinal areas are stimulated simultaneously, and each response is independently detected. Thus, a topographic ERG map may be constructed of the entire posterior pole.
- Although the origin of the components of the MERG have not been fully determined, the waveform generated by the rapid flicker (37 Hz) stimulus does represent cone function.
- The typical waveform of the basic mfERG response (also called the first-order response or first-order kernel) is a biphasic wave with an initial negative deflection followed by a positive peak . There is usually a second negative deflection after the positive peak. These three peaks are called N1, P1, and N2, respectively.

- There is evidence that **N1** includes contributions from the same cells that contribute to the a-wave of the light-adapted, full-field ERG and that **P1** and **N2** include contributions from the cells contributing to the light-adapted b-wave and oscillatory potentials.
- Although there are homologies between the mfERG waveform and the conventional ERG, the stimulation rates are higher for the mfERG and, the mfERG responses are mathematical extractions. Thus, technically the mfERG responses are not "low-amplitude ERGs". Therefore, the designations "a-wave" and "b-wave," used for full-field ERGs, are not appropriate to describe features of the mfERG waveform.





Sample mfERG trace arrays (field view) with 61 elements (panel A, left eye) and 103 elements (panel B, right eye). c, d. The 3-D response density plots (field view) associated with panels A and B

- The data of mERG can be looked at in several ways. The central area and successive rings of responses can be averaged and compared to normal.
- Of greater interest, each response can be compared to a normal response in terms of both amplitude and implicit time .
- Numerous disorders have been studied using the MERG, In patients with retinitis pigmentosa and macular degeneration, the affected areas are identified easily. But of greater importance is the ability to have an objective way to follow the progress of the disorder. Thus, the rate of loss in a patient with retinitis pigmentosa or macular degeneration may be monitored

ERG in Retinitis Pigmentosa

- In Diagnosis of RP.
- Distinguish some types of RP.
- Screening of Relatives of patient of RP.
- Follow up of disease .
- D D from other similar dystrophies.

DIAGNOSIS

- **(1) Amplitude:**

Usual ERG findings (Wide Field ERG) in RP include general reduction in the amplitude(a & b waves) of five ERG responses (rod, maximum, oscillatory, cone and flicker).

Reduction of scotopic rod response is the first ERG sign.

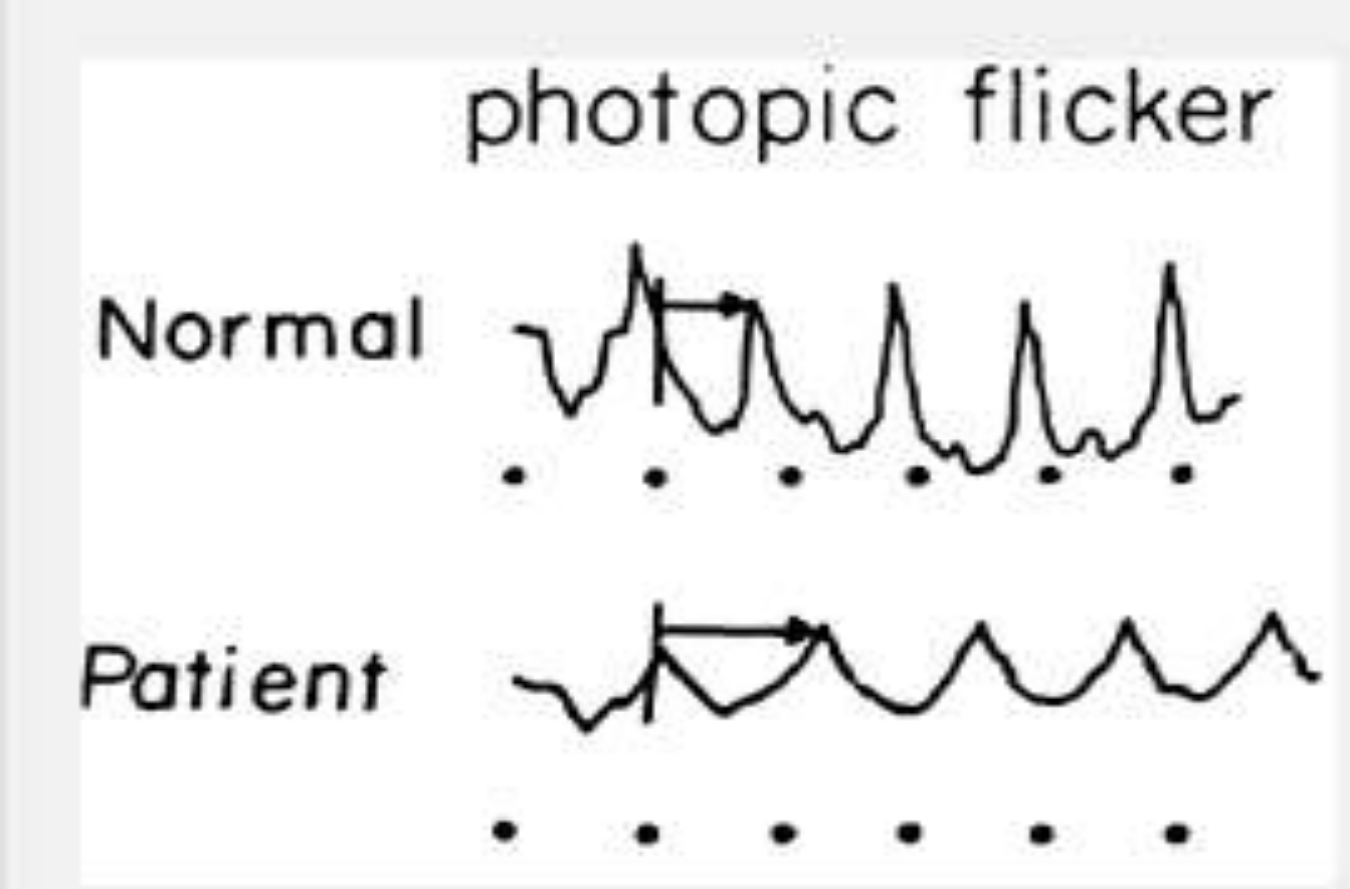
Maximum response which reflects rod and cone activity may be affected after pure scotopic responses become abnormal. Visual electrophysiologists usually concentrate on scotopic and mesopic results for early detection of RP.

- **(2) Implicit Time:**

RP patients often show prolonged b-wave implicit times. However, in the early stages of the disease, ERG may show normal amplitude and implicit time values.

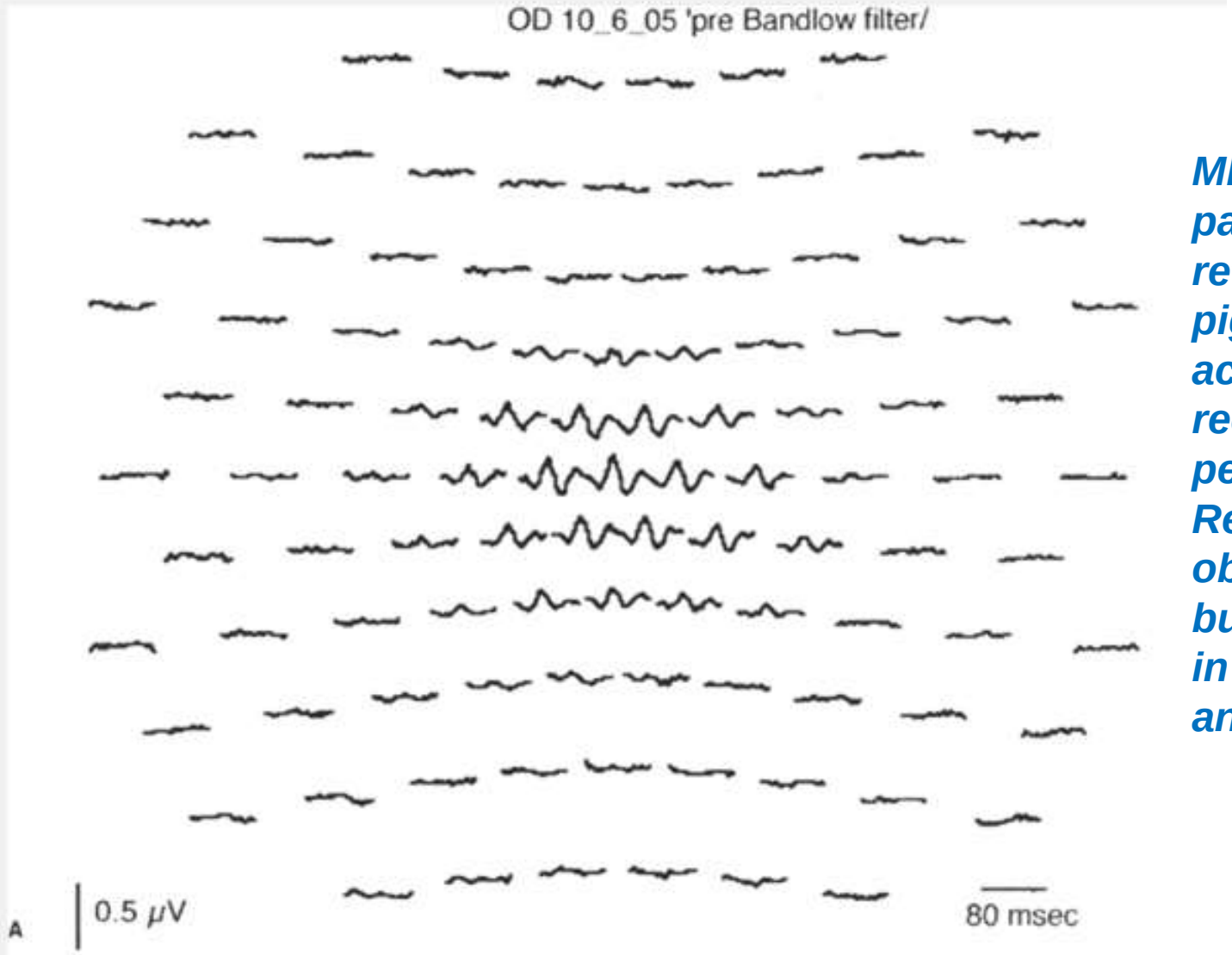
In addition to conventional ERG using time domain methods, frequency domain analysis (conversion of result of time domain to fast frequency domain ERG via special software) may be useful for diagnosis of RP. Oscillatory and flicker responses may be analyzed in frequency domain.

Fast Fourier transform may reveal two distinct high pass responses (shift to higher frequencies) in Fmod. Time and frequency domain analyses may be performed simultaneously with many modern ERG machines and may therefore be recommended in RP patients.



ERG recordings from a 14-year-old boy with documented autosomal dominant retinitis pigmentosa. His ERG shows a reduced amplitude and prolonged photopic implicit time, as compared with the normal.

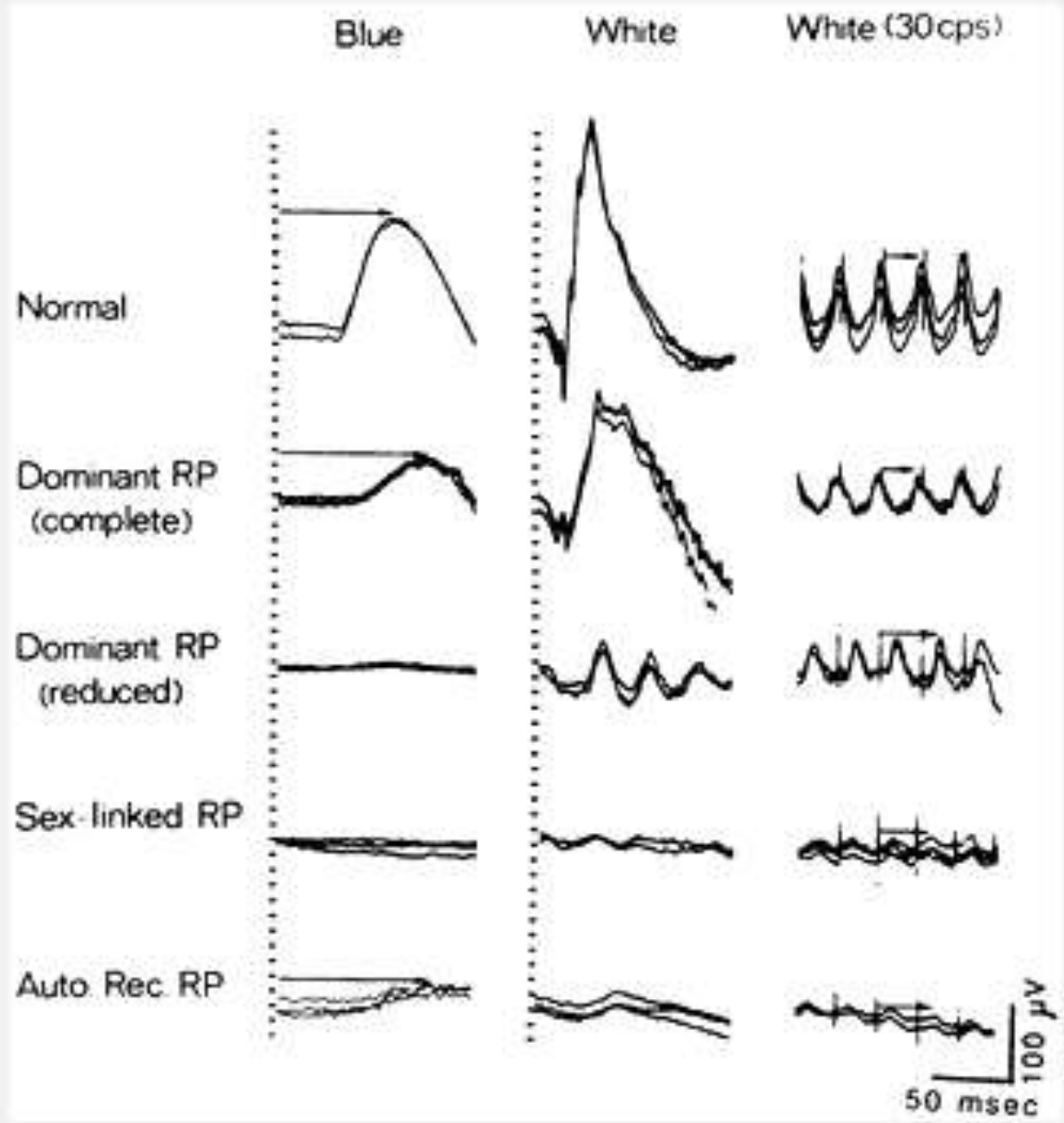
mERG in diagnosis of RP



MERG from a patient with retinitis pigmentosa. No activity is recorded in the periphery. Responses are obtained centrally, but are abnormal in both amplitude and implicit time

DISTINGUISH SOME TYPES OF RP

- Rod responses to dim blue light under dark-adapted conditions are reduced in all genetic types and, when detectable, are delayed in b-wave implicit times.
- Cone responses to 30-cycles-per-second white flickering light are normal or reduced in amplitude and normal or delayed in b-wave implicit times. In the dominant with reduced penetrance, X-linked, and autosomal recessive forms of RP, cone b-wave implicit times, are so delayed
- In the mixed cone-rod responses to single flashes of white light under dark-adapted conditions , the cornea-negative a-wave generated by the photoreceptors is reduced in amplitude in all genetic types, pointing to the involvement of the photoreceptors in these early stages
- The subnormal responses with delayed b-wave implicit times seen in the widespread progressive forms of RP contrast with the subnormal responses with normal b-wave implicit times seen in self-limited sector RP



Electroretinographic responses for a normal subject and four patients with retinitis pigmentosa (ages 13, 14, 14, and 9). Responses were obtained after 45 minutes of dark adaptation to single flashes of blue light (left column) and white light (middle column). Responses (right column) were obtained to 30-cycles-per-second (or 30-Hz) white flickering light

Screening of Relatives of patient of RP

- Full-field ERGs can be used not only to detect which patients are affected with the early stages of RP but also to determine which relatives are normal. In families with RP, patients age 6 and older with normal full-field ERGs with normal cone and rod amplitudes and normal cone and rod b-wave implicit times have not been observed to develop RP at a later time.

Follow up of disease

- Full Field ERG & mERG are used for follow up of disese.
- Focal ERG (Flash & pattern) of no value in diagnosis or follow up in RP.

D D FROM OTHER SIMILAR DYSTROPHIES

- For example; in congenital stationary night blindness:

The ERG showed a deep normal a-wave but an absent b-wave under scotopic recording conditions