Electrophysiology of the eye is a non-invasive method that allows functional assessment of retina as well as the whole visual pathway. Although there are many electrophysiological tests for assessing function of retina and visual pathway, the following protocols play a major role in the diagnosis and management of retinal disorders.

1. Full-field electroretinogram (ffERG).
2. Visual evoked potential (VEP).
3. Electrooculogram (EOG).
4. Multifocal electroretinogram (mfERG).
5. Multifocal visual evoked potential (mfVEP).
6. Pattern electroretinogram (PERG).
7. Photopic negative response (PhNR).
8. Sweep VEP (sVEP).

International Society of Clinical Electrophysiology of Vision (ISCEV) has set standards for recording each one of these tests except for photopic negative response and sweep VEP.

Multifocal electroretinogram (mfERG)

Where ffERG is a mass electrical response generated by retinal cells in response to a flash of light, mfERG stimulates various focal areas of the retina and picks up focal disease as well as maps the disease distribution. mfERG was developed by Erich Sutter.1 It is recorded monocularly using Burian Allen electrodes in a light adapted state after pupillary dilatation with refractive error correction in place. Since testing is done in a light-adapted state, the mfERG responses are primarily cone driven. It evaluates the function of fovea, parafovea and perifovea using 103 alternating white and black hexagons.

A typical mfERG waveform of the first-order kernel consists of an initial negative wave (N1) followed by a positive peak (P1) (Fig. 1). These appear similar to the ffERG photopic ‘a wave’ and ‘b wave’, but they are not identical.

The data are displayed in the form of three-dimensional topographic plots, group averages or trace arrays. Group averages and topographic plot evaluate the distribution of retinal signal. The three-dimensional plots should be seen with corresponding mfERG trace arrays for an accurate interpretation of results. Since mfERG is easy to interpret and well tolerated by the patient, it is extensively used in various hereditary retinal disorders. In congenital maculopathies like Stargardt’s macular dystrophy and Vitelliform macular dystrophy (VMD), the write foveal responses on mfERG are markedly diminished surrounded by near-normal perifoveal responses. In contrast in cone dystrophies, the mfERG-responses across the entire retina are markedly decreased or lost (Fig. 2). Role of mfERG in early stages of retinotoxicity due to various drugs such as chloroquine, hydroxychloroquine, deferoxamine and ethambutol is vital.2 It is now an integral part of...
the new standard protocol for diagnosis of retinal toxicity secondary to these drugs. MFERG can also be used as a tool for post treatment follow-up of patients with choroidal neovascular membrane or macular hole.

MFERG plays little role in optic nerve disorders because the ganglion cells do not contribute to it.

**Multifocal visual evoked potential (mfVEP)**

Flash and pattern VEP evaluate the optic nerve function. Flash VEP is mass response and pattern VEP is dominated by responses from macular area. The mfVEP as developed by Baseler et al. measures VEP responses from the focal areas of the visual field and helps in picking up distribution of the optic nerve dysfunction. Interocular comparison of mfVEP recordings is a sensitive indicator of optic nerve disease (Fig. 3). MfVEP can also be done in subjects not cooperative for visual field testing and in children.

**Photopic negative response (PhNR)**

In addition to pattern VEP, PhNR has been used as an indicator for ganglion cell function especially in early glaucomatous neuropathy. The PhNR is a slow negative potential that is seen after the b-wave of a light-adapted fERG. The background illumination and the stimulus color are altered in the basic fERG protocol to record PhNR. It can be recorded as full-field PhNR, focal PhNR and multifocal PhNR. The full-field PhNR reflects the overall retinal ganglion cell function and is used to assess the generalized optic nerve damage while focal PhNR can reflect early damage. The PhNR is found to be decreased in primary open-angle glaucoma Fig. 4, ocular hypertension and diabetic retinopathy. The PhNR amplitudes for red stimulus on blue background are large and are more effective in identifying early glaucomatous damage.

**Pattern Electroretinogram (PERG)**

PERG is helpful to differentiate between optic nerve disease and macular disorder. Transient PERG is produced by alternating reversal of a black and white checkerboard pattern at a reversal rate of 6 per second. Normal transient PERG has two main components: P50 (positive component appearing at...
45–60 ms) which shows macular function and N95 (larger negative component appearing at 90–100 ms) which shows ganglion cell function (Fig. 5). PERG has very low amplitude (0.5–8 µV); special care is needed to differentiate it from noise during recording.

It is recorded binocularly using the DTL electrodes without pupillary dilatation with refractive error correction in place. Normal fERG with decrease in P50 amplitude depicts localized macular dysfunction as seen in patients with Stargadt’s disease, macular hole and age related macular degeneration. An abnormal fERG with an abnormal PERG suggests a generalized retinal disorder as is evident in cone rod dysfunction with macular involvement. Selective reduction of N95 component, with a near normal P50 wave suggests optic nerve pathology. N95/P50 ratio remains normal in macular disease but decreases in optic nerve diseases. During acute phase of optic neuritis a profound loss of visual acuity is seen with non-recordable PERG waveforms. In chronic phase of optic neuritis as the optic nerve edema resolves P50 recovers while N95 remains abnormal with significant reduction in the N95: P50 ratio. This is because of the retrograde degeneration of the ganglion cells seen in the chronic stages of optic neuritis.7 Although PERG can differentiate between a retinal and an optic nerve disorder it does not give us the topography of the disease process.

Hence, a combination of these new investigation modalities can give us a better understanding of the physiology of the various ocular diseases and help in their management.

Fig. 4. The amplitude of PhNR (photopic negative response) is reduced in a glaucomatous (b) eye as compared to a normal waveform (a).

Fig. 5. Normal waveform of PERG showing N35, P50 and N95 components.

Fig. 6. Sweep VEP of nine different spatial frequencies. The calculated Minimal angle of resolution (MAR) based on amplitude values for different spatial frequencies (ranging from 3 to 32 cycles/degree) is 0.360 and the Snellen visual acuity is 6/13.4.
Sweep visual evoked potentials (sVEP)
The sVEP was introduced by Regan D (1973) for measuring refractive error objectively. It evaluates the visual acuity in infants, non-verbal and uncooperative children objectively. The sVEP has many spatial frequencies that are swept in single recording session within 10–15 s of duration (Fig. 6). By sweeping the spatial frequency from high to low, the visual acuity is obtained by determining the highest spatial frequency to which the visual system responds.

Conclusion
Various electrophysiological tests help in arriving at diagnosis and few tests help in the management of certain ocular diseases. mfERG assess retinal function in various retinal locations, mfVEP assess focal areas of visual pathway function, PERG help in differentiating retinal and optic nerve disorders, PhNR helps to assess ganglion cell function and sVEP is a objective quick method to quantify visual acuity.

References

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