



Jae-Jung Lee and Sung-Who Park

The electrophysiological examination is to record the electrical phenomena of the visual pathway and to determine whether the path from the retina to the visual cortex is abnormal. There are the full-field flash electroretinogram (ERG), the multifocal electroretinogram (mfERG), the pattern electroretinogram (pattern ERG or PERG), the electrooculogram (EOG), and the cortical-derived visual evoked potential (VEP). There was a lot of confusion in the interpretation of the results due to the difference in the examination environment and setting depending on the model or laboratory. Recently, the International Society of Clinical Electrophysiology for Vision (ISCEV) has provided standards for the electrophysiological examinations of the machine, the measurement method, and the interpretation and makes the examination and the reading improved in the area of ophthalmology. This chapter focuses on specific testing methods. Detailed specifications for each procedure may be found in the appropriate ISCEV standards in the homepage of www.iscev.org.

19.1 Electroretinography, ERG

Retinal function of eyes incapable of fundus exam because of corneal opacity, cataract, iris synechiae, and vitreous opacity could be evaluated by electroretinogram.

Differential diagnosis of night blindness whether progressive or non-progressive, differentiation of retinopathy similar to retinitis pigmentosa, diagnosis of non-pigmented retinitis pigmentosa, differential diagnosis of other retinal degenerations (multiple evanescent white dot syndrome, congenital stationary night blindness), and distinction between optic nerve disease and retinal disease could be evaluated by electroretinogram.

B-wave and oscillatory potential are sensitive to retinal blood circulation. Implicit time of oscillatory potential could be delayed at early phase in diabetic retinopathy. Amplitude of oscillatory potential and b-wave would be decreased in central retinal artery occlusion. Abnormality of a-wave would be helpful for discrimination of ophthalmic artery occlusion.

Generalized or localized abnormality, rod cell or cone cell abnormality, and outer retinal defect or inner retinal defect could be calculated by electroretinogram.

Visual disturbance may appear before the abnormal findings on the fundus examination, for example, the early phase of retinitis pigmentosa, drug toxicity, and diabetic retinopathy. Electroretinogram could be helpful for young

J.-J. Lee, MD.
Department of Ophthalmology, Pusan National University Hospital, Busan, South Korea

S.-W. Park, MD., PhD. (✉)
Department of Ophthalmology, Pusan National University School of Medicine, Busan, South Korea

children and psychotic. Electroretinogram is very objective test so abnormality in this test means impairment of the retina.

19.1.1 Principle and Methods

Electroretinogram detects the development of electric potentials in the retina when it is stimulated by the light (Fig. 19.1). Regardless of the conformity of the eyeballs, there is always a stationary electric current made by anode of corneal plane and cathode of posterior pole. This stationary electric current is converted to active potential by light stimulation in the retina. Serial changes of active potentials of retina could be recorded as a waveform in electroretinogram. This wave could be changed by adaptation state of the retina, angle and color of stimulated light, and duration and the location of stimulation. Amplitude of active potential is proportional to the area of the normal retina.

Sufficient pupil dilatation should be needed. Uniform stimulation to the entire retina should be motivated using Ganzfeld stimulator (Fig. 19.2). Light stimulation of 0.01 and 3.0 $\text{cd}\cdot\text{s}/\text{m}^2$ is

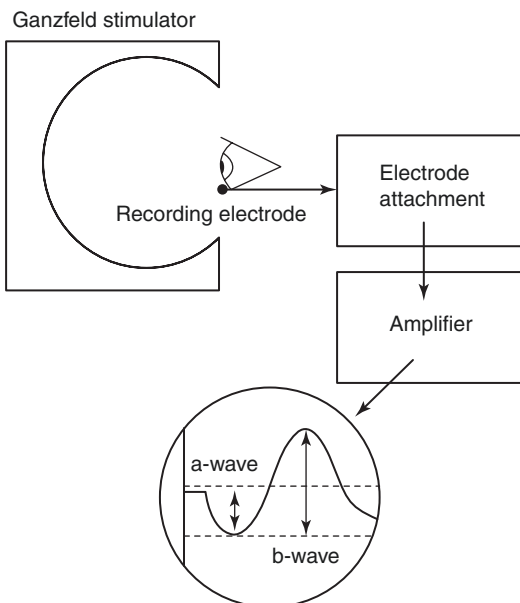


Fig. 19.1 Diagram of ERG



Fig. 19.2 Ganzfeld stimulator of ERG machine

ISCEV standards. To evaluate specific retina lesion, direct stimulator is needed for localized light stimulation. The distance between the light source and the eye should be kept constant because the intensity of the stimulated light is inversely proportional to the square of distance.

There are recording electrode, reference electrode, and ground electrode. There are many types of recording electrodes which record the change of electroretinogram by contact to the cornea or conjunctiva (Fig. 19.3). Among them, Burian-Allen contact lens is the most popular one for its safety and ease of use. Disturbance of eyelid movement is minimized because speculum and recording electrode are integrated. Reference electrode is not needed because reference electrode is attached to recording electrode. However, Burian-Allen contact lens is so expensive that it should be reused many times after disinfection. It is difficult to use for people with small eyelid gaps because the lens is large. Disposable recording electrodes called ERG jet are also widely used. It is affected by eyelid movement and has the disadvantage that the contact lens can move during the examination. Common problems for contact lens-type

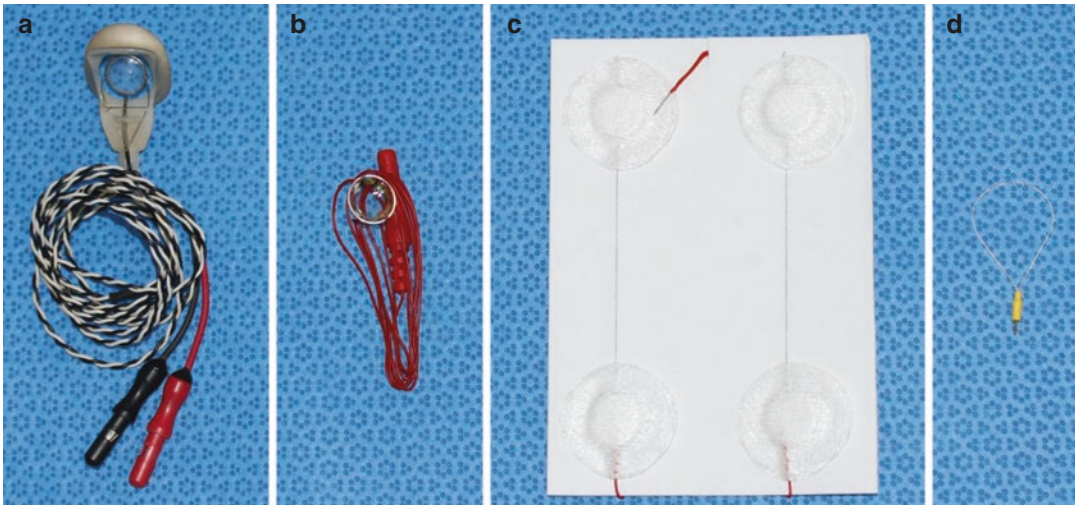


Fig. 19.3 Recording electrodes of ERG: (a) Burian-Allen electrode, (b) ERG jet, (c) DTL electrode, and (d) H-K loop

electrode are corneal abrasion and impossibility for pattern electroretinogram because of poor clarity. DTL electrode and skin electrode could be used for children.

Full dilatation of the pupil is needed. Smoking is prohibited during examination because it affects the waveform. Children with poor cooperation should be put to sleep while testing. Alcohol or Skinpore is applied to the skin for removal of oily material, and electrode is attached tightly with electrode glue. Reference electrode as anode is placed at both lateral canthal areas where ISCEV recommends. Ground electrode is attached to the forehead or earlobe. Electrode should be blocked against the light because of photoelectric effect.

Dark adaptation should be done sufficiently 20 min or more. Over 30 min of dark adaptation is needed if the patient is tested immediately after being in bright outdoors. After dark adaptation, cathode contact lens is applied with methylcellulose after topical anesthesia under dim red light. For children, pediatric corneal electrode or skin electrode should be prepared. Dark-adapted 0.01 ERG, dark-adapted 3.0 ERG, and dark-adapted 3.0 oscillatory potential are recorded respectively. Light adaptation should be done over 10 min. Light-adapted 3.0 ERG and light-adapted 3.0 flicker ERG are recorded.

19.1.2 Characteristics of ERG Waveform and Its Origin

Electricity flows through resistance by voltage difference. Electricity in ERG develops in retinal cells. Extracellular fluid and vitreous play a role as resistance (Fig. 19.4). Photoreceptor consists of cone and rod cell and its characteristics are shown in Table 19.1. Standard ERG waveform, amplitude and the definition of implicit time are noted in Fig. 19.5.

19.1.2.1 A-Wave

A-wave is the first negative wave which reflects the function of photoreceptors. Rod cell potential is not shown in ERG because it decreases and recovers so slowly that it is obscured by b-wave. Cone cell potential decreases and increases so rapidly that definite negative wave is recorded on the 3.0 cd•s/m² stimulation. Amplitude of a-wave is defined as the difference between reference potential and the peak of negative potential (Fig. 19.5).

19.1.2.2 B-Wave

B-wave is positive wave which appears after a-wave originates from bipolar cell. Amplitude of b-wave is defined as difference between the trough of the a-wave and the peak of the b-wave (Fig. 19.5).

Fig. 19.4 Retinal layers and the origin of development of each electric potential

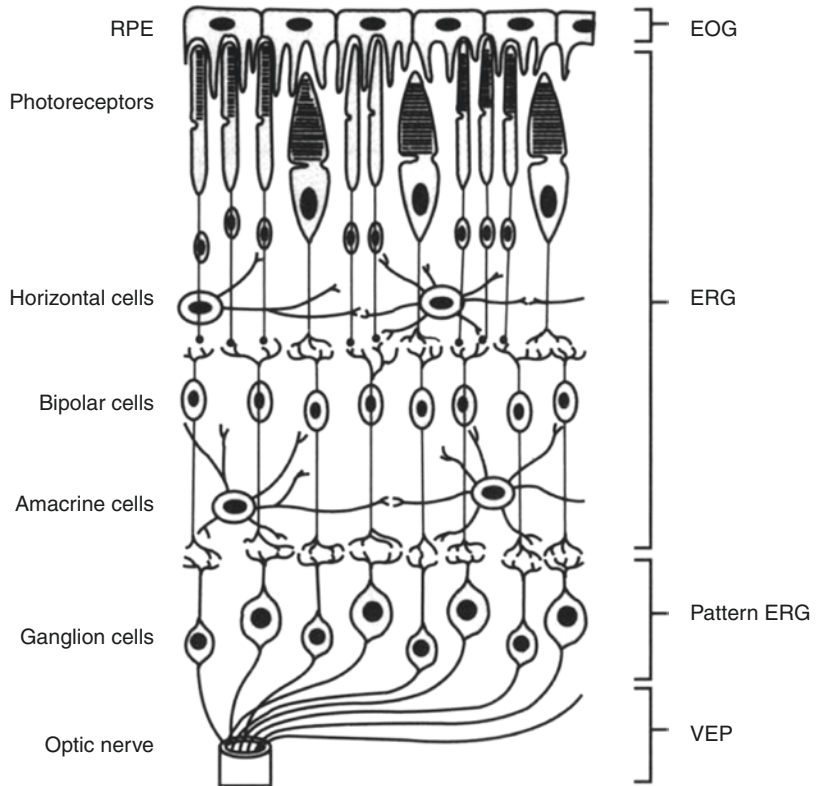


Table 19.1 Characteristics of cone and rod cell

	Cone cell	Rod cell
Color	Recognition	Unrecognition
Vision in darkness	Bad	Good
Maximal intensity location	Fovea	15–20° from the fovea
Number of cells	7,000,000	120,000,000
Sensitivity difference according to stimulus direction	Recognition	Unrecognition
Maximal sensitivity wavelength	555 nm	510 nm
Stimulus frequency of fused flicker	High	Low

19.1.2.3 Oscillatory Potential

Oscillatory potential is a duplicated wave shown at the elevation part of b-wave. It can be separated by filtering high-frequency wave and low-frequency wave. This small wavy electricity is induced from inner plexiform layer and originated from negative feedback by amacrine cell. It is clearly shown when cone cell and rod cell are simultaneously stimulated by 3.0 cd•s/m² stimulation in dark adaptation (Fig. 19.5).

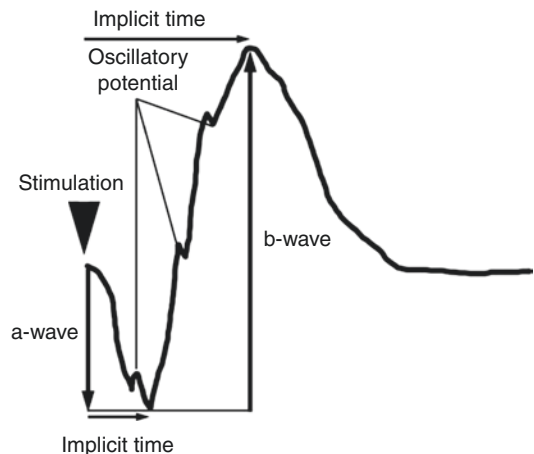


Fig. 19.5 ERG a- and b-wave, amplitude, and implicit time

19.1.2.4 Early Receptor Potential

When the stimulated light is very strong, minute potential change derived from outer segment of photoreceptor at the beginning downward part of a-wave is observed. It is not shown in standard ERG and is confused with wave generated by photoelectric effect using metallic recording electrode.

19.1.2.5 C-Wave and Off-Effect

With long stimulation light, c-wave appears after b-wave, and off-effect of c-wave is recorded at the end of light stimulation.

19.1.3 Standard Electroretinogram (ISCEV 2015)

Standard ERG is performed in dome-shaped visual field stimulation device. Uniform light is illuminated to central retina 120° and the following five tests are performed (Fig. 19.6).

19.1.3.1 Dark-Adapted 0.01 ERG

Dark-adapted 0.01 ERG is previously called as scotopic ERG. This is the examination for detection of rod response. Minimum 20 min of dark adaptation is needed, and $0.01 \text{ cd}\cdot\text{s}/\text{m}^2$ white flash light lower than the threshold of cone cell is evoked. Interval between flash lights is minimum 2 s. A-wave is not shown and large b-wave appears.

19.1.3.2 Dark-Adapted 3.0 ERG

Dark-adapted 3.0 ERG is also called as maximal combined response. When $3.0 \text{ cd}\cdot\text{s}/\text{m}^2$ white flash light is applied after dark adaptation, a-wave including cone cell and rod cell and maximal b-wave are acquired. Interval between stimulation is minimum 10 s.

19.1.3.3 Dark-Adapted 10 ERG

In comparison with the dark-adapted 3 ERG, the dark-adapted 10 ERG is characterized by a larger a-wave with better definition of peak time, greater distinction of negative ERG waveforms, and enhanced oscillatory potential amplitudes. In addition, this ERG may give more reliable responses in patients with opaque media or immature retinae. The dark-adapted 10 ERG should be recorded after the dark-adapted 3.0 ERG, with an interval of at least 20 s between strong flash stimuli.

19.1.3.4 Dark-Adapted Oscillatory Potential

Dark-adapted oscillatory potential is simply called as oscillatory potential. After dark adaptation, cone cell and rod cell are simultaneously stimulated with $3.0 \text{ cd}\cdot\text{s}/\text{m}^2$ white flash light, and interval between stimulations is minimum 15 s. Duplicated wave which appears at upper line of b-wave is separated by electric filter.

19.1.3.5 Light-Adapted 3.0 ERG

Light-adapted 3.0 ERG is called as photopic ERG or single flash cone response. After light adaptation, rod cell response is suppressed by $30 \text{ cd}/\text{m}^2$ background light, and $3.0 \text{ cd}\cdot\text{s}/\text{m}^2$ white flash light is used for recording.

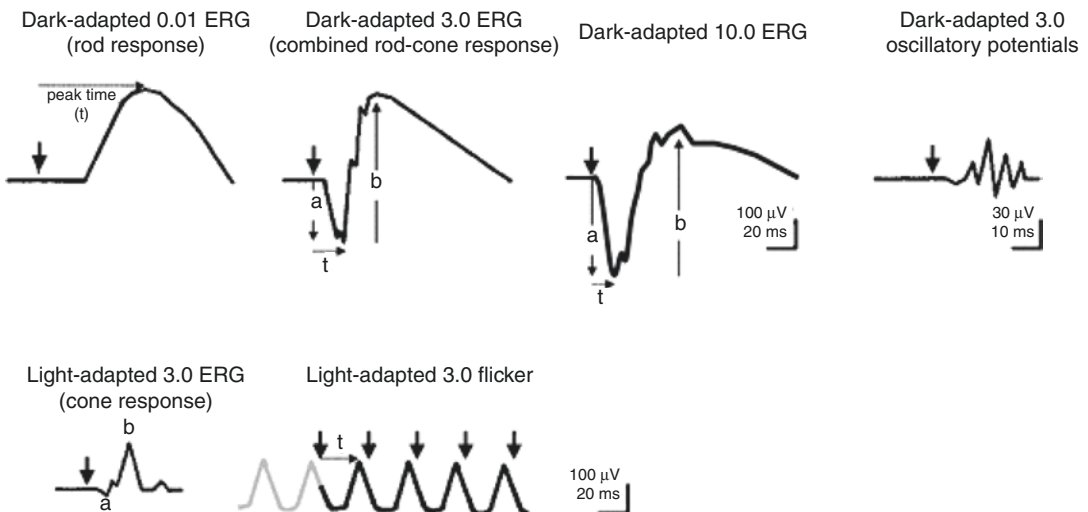


Fig. 19.6 ISCEV standard (ISCEV standard 2015 update)

19.1.3.6 Light-Adapted 3.0 Flicker

Light-adapted 3.0 flicker is previously called 30 Hz flicker. Rod cell can respond to stimulation below 20 Hz but cannot respond to stimulation over 30 Hz. Cone cell response can be selectively assessed by this feature. Classic sign waveform is shown, and a-wave and b-wave are not distinguished.

19.1.4 Abnormal Findings

The activity of nerve fiber layer and efferent inhibitory fiber of optic nerve are not recorded in ERG. Retinal vascularity and various nerve fiber circuits should be considered when analyzing ERG. ERG recording is the result from the entire retinal response, not localized response that lesion larger than 3 disc diameter is needed for changing recordings in ERG. B-wave and oscillatory potential may show abnormalities if there is photoreceptor abnormality, even if the bipolar cells or amacrine cells in the inner retina are normal.

Noise can be developed by poor attachment of electrode or problem with connecting electrode. Non-recordable waveform could be pathologic, but connecting status of electric line, problem with recording, or mechanical problem should be checked. Eyeball movement and photoelectric effect could make disturbed waves.

Strong stimulation light makes increment of amplitude and shortens implicit time. Dark adaptation time can affect the result but no change after 15 min. Effect of pupil diameter increases in weak stimulation. Ganzfeld stimulator is recommended for uniform stimulation on large area because the size of stimulated area can influence the result. Refractive error could be neglected except severe high myopia. Age can affect the result, and infant and old people show decrease of amplitude in a- and b-wave and elongation of implicit time.

19.1.4.1 Types of Abnormal ERG
(Fig. 19.7)

Currently used ERG classification is determined according to relative relationship between a-wave

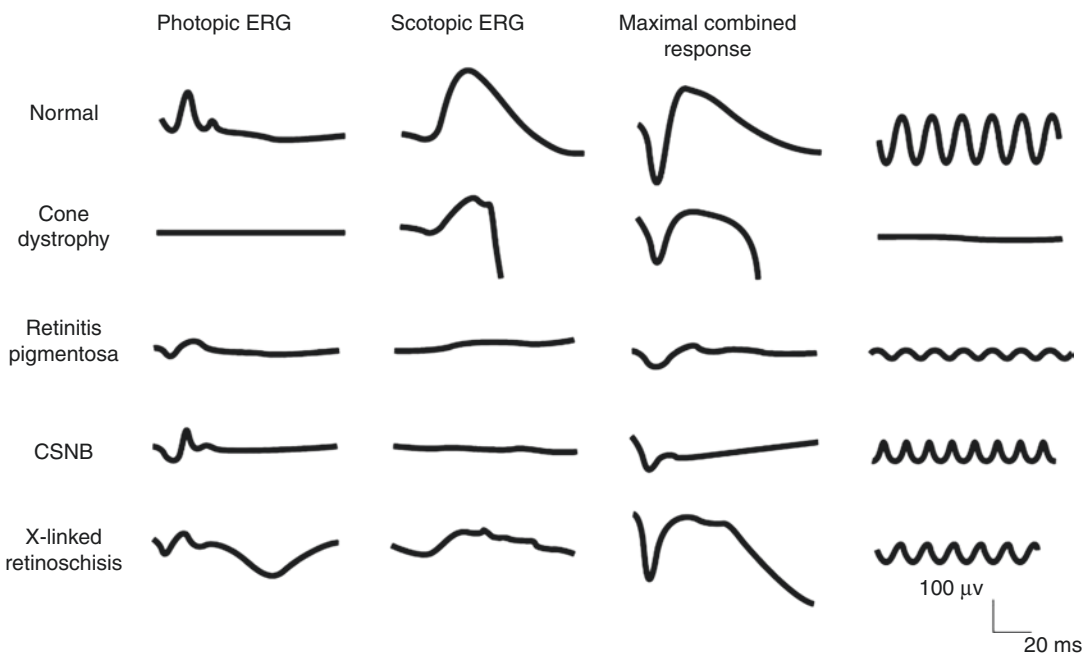


Fig. 19.7 Various ERG findings according to the type of disease

and b-wave. B-wave is selectively decreased in inner plexiform layer diseases.

Supernormal means that b-wave enlarged abnormally. This includes early phase of siderosis bulbi, hypertensive retinopathy, use of hallucinating drugs, and optic nerve atrophy.

Subnormal means that amplitudes of all waves are decreased over 30% difference compared to normal response and over 0.18 mV difference between both eyes. Diffuse retinal abnormality such as retinitis pigmentosa and localized retinal detachment shows subnormal.

Negative ERG means amplitude of b-wave is larger than a-wave ($b/a < 1$). Positive wave after a-wave cannot reach to early potential. Severe abnormality in middle retinal layer including bipolar cell shows negative ERG. This includes X-linked retinoschisis, central retinal artery occlusion, congenital stationary night blindness, quinidine toxicity, and Oguchi disease.

Non-recordable means no retinal function. This includes end-stage retinitis pigmentosa, total retinal detachment, ophthalmic artery occlusion, and Leber congenital night blindness.

Cone cell dystrophy shows subnormal scotopic ERG, but photopic ERG and flicker are selectively decreased or lost. Oscillatory potential abnormality represents decrease or loss of oscillatory potential or elongation of implicit time. This includes diabetic retinopathy and retinal artery occlusion.

19.1.5 Others

19.1.5.1 Focal ERG

Seven percent of cone cell presents in central macula that full-field ERG in age-related macular degeneration shows normal. Localized stimulation to macula is needed for analyzing macular function. Specific stimulator retinoscopy is used for examining posterior pole. First, rod cell is suppressed outside 10° from the fovea by bright light, and then 42 Hz rapid flickering white flash light is given to 4° area around the fovea. Hundreds of small focal ERG are recorded and analyzed in general.

19.1.5.2 Strong Flash ERG

Light stimulus stronger than standard flash is used for examination, and it is useful for eyes with media opacity.

19.2 Multifocal ERG, mfERG

In general, electroretinogram (ERG) is the response of the entire retina to stimulated light that it is not appropriate for the evaluation of localized retinal lesions. Focal ERG was developed to examine the localized retinal lesion to compensate for these shortcomings, but it is not commonly used because of difficulties in recording. Therefore, a new method known as VERIS (Visual Evoked Response Imaging System) to simultaneously record the multiple focal lesions on the retina was developed by Sutter et al. This device stimulates the posterior pole of retina with pre-calculated pattern at the same time, and focal ERG at each retinal lesion is computed and separated in a short time. The extent of disability is measured objectively in a short time.

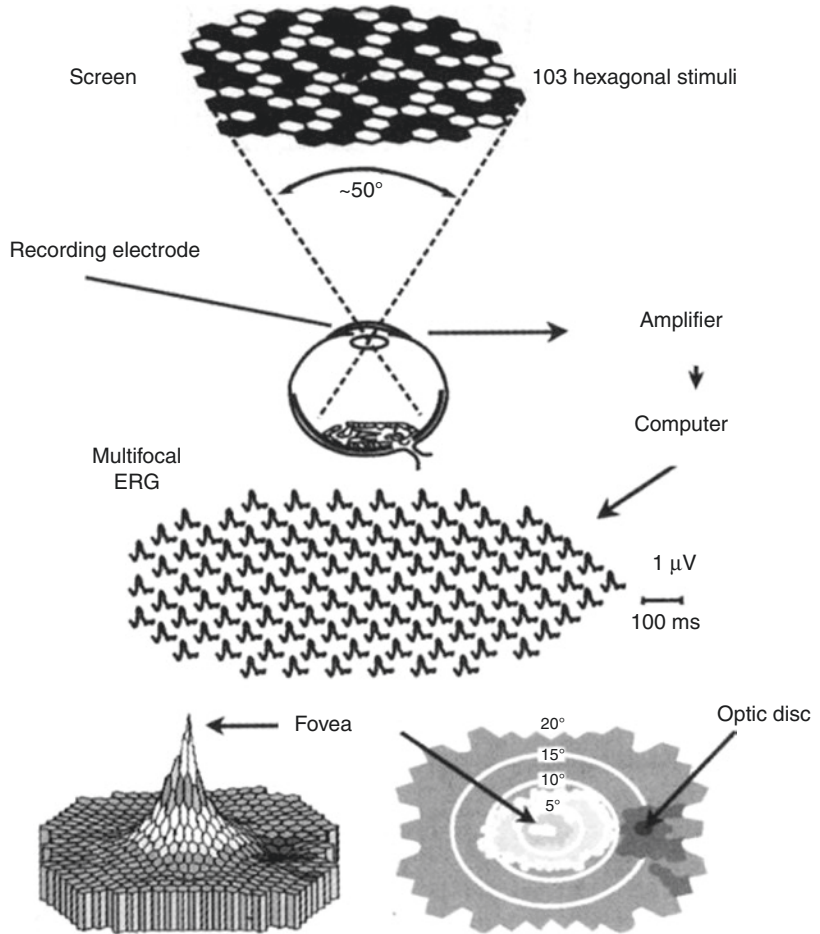
The measured visual field is about $40\text{--}50^\circ$ in diameter and 61 or 103 hexagonal stimuli are used in general. Two hundred forty-one hexagonal stimuli are used for very accurate result, but proper cooperation is needed because the examination time is very long. Half the black and white on the hexagon, it looks irregular but stimulates according to pre-defined rules (pseudo-random), and ERG of each hexagon is calculated from this current signal (Fig. 19.8). The area of the hexagon is small in the center and large in the periphery for the same amplitude of the recorded focal ERG in each region of the normal person.

Electric potential of corresponding macular lesion is not directly measured and obtained by calculation that the result can be affected by variable factors. Therefore, ISCEV standard was published in 2011.

Multifocal ERG can be used for the following diseases.

Retinal disease without fundus changes: Hereditary retinal diseases are occult macular dystrophy and Stargardt disease. Acquired retinal diseases are acute zonal occult outer retinopathy

Fig. 19.8 Multifocal ERG wave, amplitude, and implicit time



(AZOOR), white dot syndrome, and acute idiopathic blind syndrome.

- Differentiation between optic nerve disease and retinal disease
- Evaluation of visual function before and after surgery of macular disease
- Evaluation of localized cone cell function in various retinal diseases

19.2.1 Method

After pupil dilatation, dedicated contact lens electrode is applied with local anesthesia. The contralateral eye should be occluded.

Correct visual acuity with refractive lens while the contact lens electrode is applied.

Finely adjust examination distance with corrected visual acuity.

Reference electrode is attached to both lateral canthal areas except anode recording electrode. Ground electrode is attached to the ipsilateral earlobe.

Patient's face is placed on the chin rest and center point of the monitor should be watched.

After starting the exam, the patient should keep watching the center point even though the stimulus of the monitor changes rapidly.

Total examination time takes about 4 min but the inspection process is difficult, and it is not easy to maintain concentration. Patient usually rests every 30 s and test is divided into eight sessions.

Test should be done again if there are a lot of noises due to eye movements or eye flicker.

19.2.2 Interpretation

Multifocal ERG is based on the response of cone cell. Standard waveform is two negative waves (N1, N2) and one positive wave (P1) (Fig. 19.9a). ERG corresponding to each hexagonal stimulus is shown with corresponding visual field test.

The amplitude of P1 and implicit time are shown as a three-dimensional (3D) topographic map. 3D topographic map of amplitude provides the amplitude of retina as height/area. The center area has the highest amplitude, whereas the peripheral area has lower amplitude because the area of the central

hexagon is the smallest in normal individual. It must be interpreted by referring the trace array in which individual waveforms are recorded because noise can be displayed in a 3D topographic map. The difference between the normal value and the patient's result can be displayed as a topographic map depending on the model. Depressed region means decreased retinal function. ERG abnormality corresponding to abnormal visual field is assumed that the visual field defect is due to retinal disease (Fig. 19.10). If the result is normal, optic nerve or central nervous system (CNS) disease would be suspicious rather than retinal disease.

Fig. 19.9 Normal finding of multifocal ERG: (a) ISCEV standard of multifocal ERG, 2011 update, (b) 3D topographic map of trace array and amplitude of normal multifocal ERG

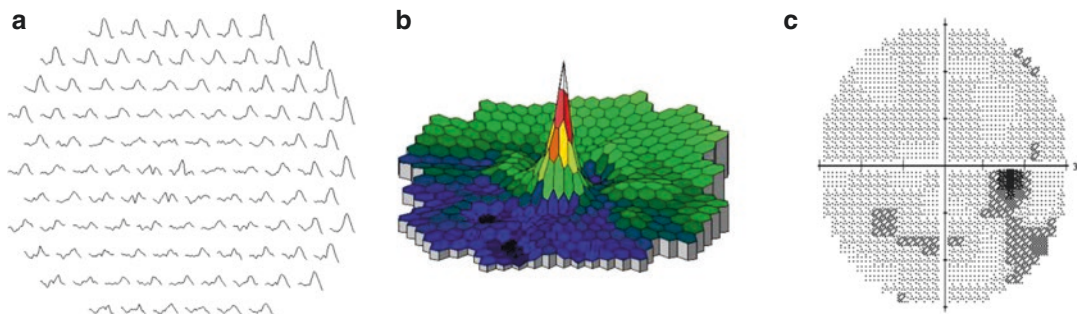
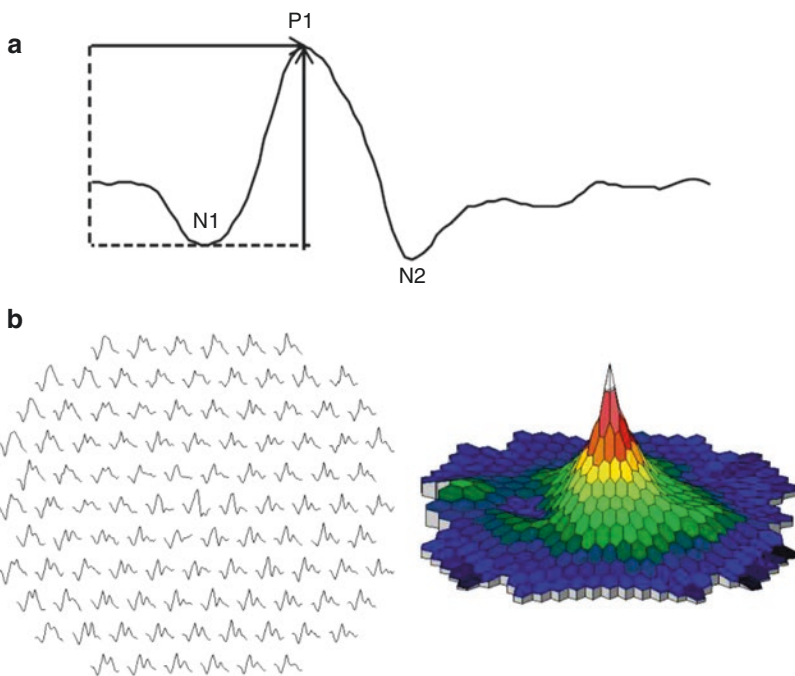


Fig. 19.10 Multifocal ERG and visual field defect in patient with acute zonal occult outer retinopathy: (a) trace array, (b) 3D topographic map of amplitude, (c) visual field test

Hexagonal potentials in ring shape from the center to the periphery are averaged, and the fovea is divided into four quadrants, and the average potential of each quadrant is displayed.

19.3 Pattern ERG

Pattern ERG is related to macular function which is the response of retinal ganglion cell. It is useful for early diagnosis of glaucoma and evaluation of progression. Abnormality in pattern ERG is used for discrimination of optic nerve disease or macular disease.

19.3.1 Method

Visual acuity is corrected with patient's glasses or trial lens set without pupil dilatation. Multifocal glasses should be avoided. Fluorescein angiography or fundus photo should be avoided before the test, but if already done, 30 min interval is needed. Contact lens electrode is inadequate for recording electrode due to blurred vision, and DTL electrode which is inserted to conjunctival sac or roof electrode is suitable.

The size of each rectangle in pattern is 0.8° (0.2°). The width and height of the entire stimulus should be 15° (3°) and aspect ratio should be between 4:3 and 1:1. The luminance of the white square is 80 cd/m^2 or more. Conventional CRT monitors can be widely used, but LCD monitor is needed to reduce the errors in luminance. The black and white contrast is better when closer to 100% and should be at least 80%. It inverts 4 ± 0.8 times per second ($2 \pm 0.4 \text{ Hz}$). Recording and reporting should use reversal per second (rps) rather than Hz. Both eyes should be examined at the same time. Pattern ERG should be performed for one eye at a time when visual evoked potential is scheduled to be done at the same time.

Pupil dilatation should not be done, and test is done with corrected vision. Pupil size should be recorded.

Recording electrode is located past the inside of the lower conjunctival sac, and roof electrode should not be in contact with cornea.

Reference electrode is attached to both lateral canthal areas. Ground electrode is attached to the forehead but other parts are also possible.

The central retina is tested with check pattern stimulus alternating black and white. Center point of the monitor should be watched. Eye flicker should be avoided during examination, and it is better to stop the test for a while when it is difficult to avoid eye flicker.

Recorded responses of at least 100 stimuli are averaged. Over 300 stimuli are needed to find a slight change or if there are a lot of background noises.

19.3.2 Interpretation

Distinct single positive wave (P50) and two negative waves (N35, N95) are recorded (Fig. 19.11). P50 and N95 are used for analysis because N35 is prone to error. Amplitude of P50 and N95 and implicit time are recorded and reported. Amplitude of P50 is calculated by the difference between minimum of N35 and maximum of P50. If N35 is not clearly observed, it is calculated from the average potential from the zero point to the point at which P50 starts to the maximum point of P50. Amplitude of N95 is calculated by the difference between maximum of P50 and minimum of N95. Implicit time of P50 is 45–60 ms and amplitude is generally $2.0\text{--}6.0 \mu\text{V}$ in normal person. Implicit time of N95 is 90–100 ms.

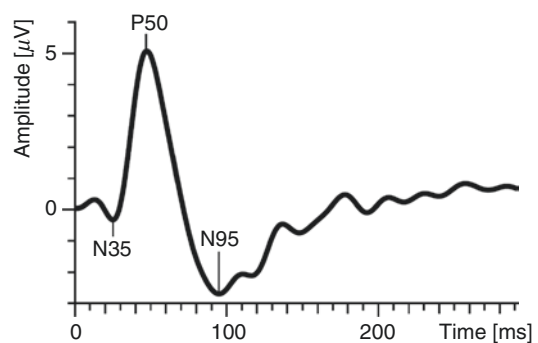


Fig. 19.11 Normal pattern ERG that shows N35, P50, and N95. (ISCEV standard, 2012 update)

19.4 Visual Evoked Potential, VEP

Visual evoked potential (VEP) is a computer averaged response of the nervous system to sensory stimuli, used for examining function of visual pathway from the sensory organs to the central nervous system. VEP is the recording of response of the central nervous system when giving the visual stimulus. ISCEV standard is revised in 2016, and the main changes in this revision are the acknowledgment that pattern stimuli can be produced using a variety of technologies (Fig. 19.12).

VEP is used for examination of the retinal pathway from retinal ganglion cell to the occipital lobe. Visual acuity level is considered in the interpretation of the results because it reflects the macular function. Pattern stimulus reflects central retinal function that it could be used for evaluating central vision.

Optic nerve diseases, optic radiation disease, evaluation of potential visual acuity with invisible fundus due to corneal opacity, cataract and vitreous opacity, unknown cause for

decreased vision, and pediatric visual function test with poor cooperation could be evaluated by VEP.

It is known that the light stimulus to the retina or alternating black and white check pattern can induce visual evoked potential (Fig. 19.13). These evoked potentials appear as variable waveforms, and they affect each other by the anatomy and physiological structure or condition of visual pathway. Neurophysiological abnormalities can be assessed by determining the shape of these evoked potential waveforms and the time and amplitude of reaching the peak after stimulation.

Various kinds of visual evoked potential can be measured by visual stimulation. Pattern reversal VEP and flash VEP are the most widely used. Pattern reversal VEP is correlated to 17 area of brain and flash VEP is associated with 18 and 19 areas of brain. Pattern reversal VEP is basically used and flash VEP is performed with media opacity and visual acuity below 0.1. Pattern onset/offset VEP is added to standard test on revised ISCEV standard.

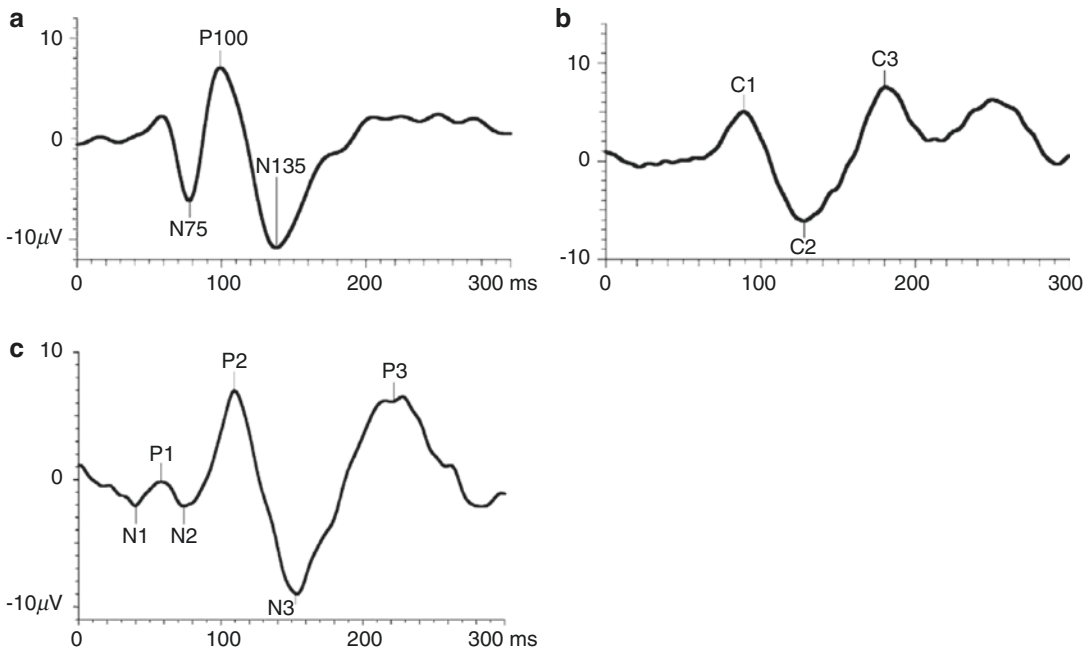


Fig. 19.12 Normal VEP: (a) pattern reversal VEP, (b) pattern onset/offset VEP, (c) flash VEP (ISCEV standard, 2016 update)

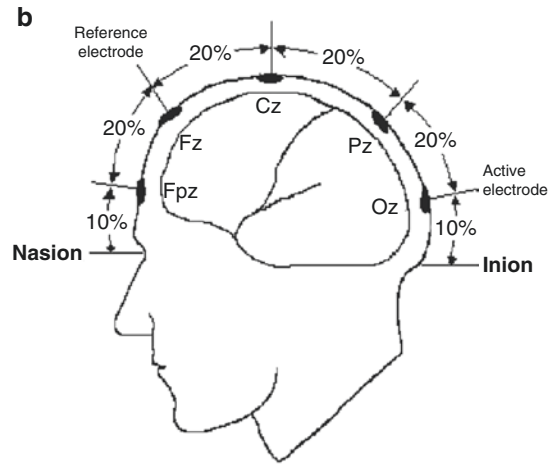
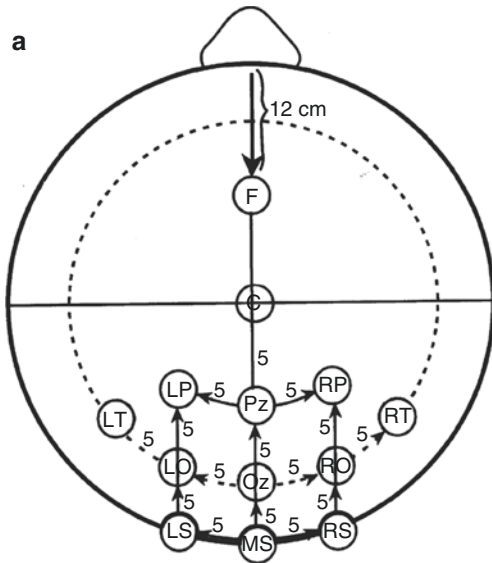


Fig. 19.13 Electrode attachment site of VEP: (a) F frontal, O occipital, P parietal, S suboccipital, T temporal, C vertex, L left, R right, M middle (a) Z means midline.

(b) Find the electrode attachment position as a percentage of distance from the nasion to inion

19.4.1 Pattern Reversal VEP

Pattern reversal VEP can be used for visual pathway defect, especially optic nerve disease; diagnosis of demyelinated disease, retrobulbar optic neuritis, ischemic optic neuropathy, and compressive optic neuropathy; and also assessment of objective visual acuity: pediatric visual function, psychogenic visual impairment, and differentiation of malingering.

It is stimulated by alternating black and white check pattern. Average luminance should be 50 (40–60) cd/m². Contrast sensitivity should be at least 80%. The size of each rectangle is used more than one including 1° and 15 min; total visual field of the stimulus is minimum 15°. The alternating speed is used twice per second (1.0 Hz, ±10%). Visual angle of each pattern, alternating frequency, alternating time, average luminance, pattern contrast, and visual field size are reported.

Normally, the amplitude and implicit time of the maximum negative wave N2 (or N75) after 75 m/s after stimulation and maximum positive wave P2 (or P100) after 100 m/s after stimulation are calculated (Fig. 19.12). It is easier to detect

and measure than flash VEP and waveform is more consistent. Implicit time of P100 is the most important variable since there is a small error between individuals and between eyes and examinations.

19.4.2 Pattern Onset/Offset VEP

Discrimination of malingering and patient with nystagmus can be evaluated by pattern onset/offset VEP.

Pattern and diffuse background are stimulated alternately. The condition of the pattern is the same as the pattern reversal stimulus. The luminance of diffuse background is set equal to the average luminance. The time when the pattern appears is recommended as 200 ms and diffuse background appears is recommended as 400 ms. The response is recorded when the pattern appears on diffuse background.

Individual difference is greater than pattern reversal VEP but it has less error due to poor cooperation. Three waves appear in normal (C1, C2, and C3). C1 is positive wave which is recorded near 75 ms. C2 is negative wave near

125 ms. C3 is positive wave near 150 ms (Fig. 19.12). Each amplitude is calculated by the difference between the maximum and minimum of the front wave.

19.4.3 Flash VEP

Flash VEP can be used when the pattern stimulus cannot be focused on the retina due to media opacity such as corneal opacity, cataract and vitreous opacity, poor cooperation in young children, and visual acuity below 0.1 with non-response to pattern stimulus such as macular degeneration disease, macular hypoplasia, visual development delay, cortical blindness, etc.

At least 20° of flash stimulation should be given. Light stimulus is at least 3 cd·s/m² in a room with dim light. Screen or full-field stimulating device can be used. The frequency of light stimulation should be 1 per second (1.0 Hz ± 10%).

It is useful in patients with media opacity. Two positive waves and two negative waves (N1, P1, N2, P2) appeared and maximal positive wave P2 appears after 95–120 m/s (Fig. 19.12). The abnormal findings are shown as delayed response, loss of waveform, and decreased amplitude, but there is a big individual difference that it is common to evaluate the difference between the right and left eye. Each laboratory should have normal range data of the measurements.

19.4.3.1 Method

Correct the refractive error and attach the electrode. Resistance of electrode should be below 5000. There are various methods depending on the attachment sites; a reference electrode is generally attached to the midline frontal (Fz) above 12 cm from the nasion, and a recording electrode is attached to the midline occipital (Oz) above 5 cm from theinion and on its left and right 2.5–5 cm (right occipital, RO; left occipital, LO). Ground electrode is attached to the forehead, parietal area (Cz), earlobe (A1 or A2), or the mastoid process (Fig. 19.13).

Visual stimulus should be given with occluding one eye. Distance between visual stimulus and the patient should be kept 100 cm.

Recording range is adjusted to 1–300 Hz and 10–100 Hz is used in general. After visual stimulation, EEG response is recorded after 150–200 averaging procedures using a computer. At least three channels (RO-MF, MO-MF, LO-MF) should be recorded and recording time is 250 m/s.

Contralateral eye is covered and recorded again.

Brightness, contrast, stimulus range, size and location, status of examiner, sex, and age can affect the result. Especially, flash VEP is very difficult to compare with a normal person because there is a big individual difference. But the difference of response between both eyes is less than 10%, and both eyes should be compared to determine abnormality.

All examinations should be done in constant luminance indoor and outdoor. As the lightning of the room becomes bright, the intensity of the stimulus decreases that P100 (P2) implicit time elongates. Lighting of the retina according to pupil size should also be considered. Test result is different depending on the degree of contrast of the lightness and darkness of the pattern. The implicit time of P100 is delayed and the amplitude is decreased with low contrast.

Based on a constant size of stimulus range, the smaller the size of the pattern of black and white check, the wider the amplitude. For P2 implicit time, there is no difference in the range of stimulation over 8°, but it elongates in a small stimulus range of 8° or less. It is more prominent in large pattern. Central 8° is projected to 17 area which is apex of the occipital lobe and outside 8–32° is projected to visual cortex. Implicit time of flash VEP P2 is 10% longer than pattern reversal VEP P100.

There is a slight difference depending on fixation, visual acuity, and pupil size. Waveform abnormalities might occur without optic nerve disease if the patient is not focused on the central point on the monitor. N75 disappears and implicit time to P100 elongates in a patient with blurred vision with inadequate correction. Therefore, pattern reversal VEP should be done after correction of visual acuity. For adult with poor cooperation, child, or during the surgery, flash

VEP could be used. Implicit time to P100 elongates with age. Males have larger amplitudes and shorter implicit times than females.

19.4.3.2 Abnormal Findings

VEP result is closely related to macula status. If the fundus examination shows abnormality of the macula, the information obtained by VEP is limited. Therefore, VEP is performed to evaluate the abnormality of the visual pathway with normal fundus finding and also used to investigate the potential for visual recovery in cases where fundus examination is not possible. Early diagnosis prior to optic nerve abnormality in multiple sclerosis, visual pathway disease, infant, or, where communication is not possible, VEP is useful for vision assessment and visual field impairment.

In cases of non-recordable, P100 (P2) delay compared to normal range, P100 (P2) difference between the right and left eye more than 10% or 9 m/s, and P100 delay 118 m/s or more in pattern reversal VEP, it can be suspected as lesions of optic nerve, optic radiation, or visual pathway posterior to optic radiation (Fig. 19.14).

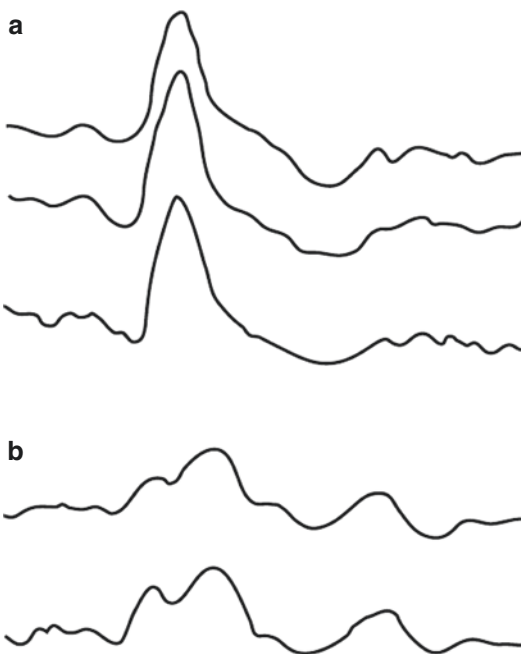


Fig. 19.14 VEP in normal and optic neuritis (multiple sclerosis) patient: (a) normal and (b) optic neuritis (multiple sclerosis) patient

19.5 Electrooculography, EOG

It is an assessment of retinal pigment epithelium (RPE) function and useful for distinguishing RPE disease with normal ERG and abnormal EOG. The most typical disease is the Best disease. But a lot of neuroretinal diseases could be shown as RPE abnormality with disease progression. Therefore, EOG abnormalities could be seen as the disease progresses.

EOG is useful for the following diseases:

Bestrophine gene abnormality: Best disease, autosomal recessive bestrophinopathy, autosomal dominant vitreoretinopathopathy (AD-VIRC)

Multiple evanescent white dot syndrome (MEWDS), acute zonal occult outer retinopathy (AZOOR), acute idiopathic blind spot enlargement (AIBSE) syndrome

Choroidal circulation disorder, ocular ischemic syndrome

For geographic chorioretinitis, early retinitis pigmentosa, Stargardt disease, choroideremia, chorioretinal gyrate atrophy, central retinal artery occlusion, chloroquine retinopathy, pattern dystrophy or butterfly dystrophy, cone cell dystrophy, abnormal value could be shown according to the disease progression.

As mentioned above, there is a potential difference between the anterior and posterior segment of the eyeball; it is called as a static potential. The cornea and lens do not respond to light but the potential of RPE varies according to the variation of surround brightness. It decreases in dark adaptation and increases in light adaptation. In accordance with this finding, EOG decreases in dark adaptation and increases in light adaptation. To record the normal EOG, adhesion status of RPE and photoreceptor and normal circulation of the retina and choroid are needed. If one of them is missing, EOG result can be changed. Both EOG and ERG should be performed clinically for evaluating pathophysiology of various retinal diseases, especially for evaluation of RPE function because normal ERG does not reflect the RPE activity.

19.5.1 Method

Patient should be in ordinary room lighting more than 1 h before examination, and fundus photography is prohibited during this period. Full dilation of pupil is needed. ISCEV recommends 7 mm pupil dilatation. The size of pupil is recorded and the lighting should be brighter when dilation is not enough. For example, a 5 mm pupil needs twice the brightness to get the same retinal response. Each electrode is attached to the medial and lateral canthal area. Reference electrode is attached to the forehead.

Under a room lighting of constant brightness, EOG can be measured in either method; the horizontal eye movement is performed in a rhythmic manner along two moving red lights within 30° horizontal range or looking at two flashing red lights at intervals of 6 times/min (1 time per 10 s) located at 30° apart from each other. EOG is measured for several minutes (Fig. 19.15). If amplitude obtained is stable, it is called base value. If noise is recorded, every electrode should be checked again.

Recording begins after 15 min of dark adaptation. EOG is measured once per minute. The

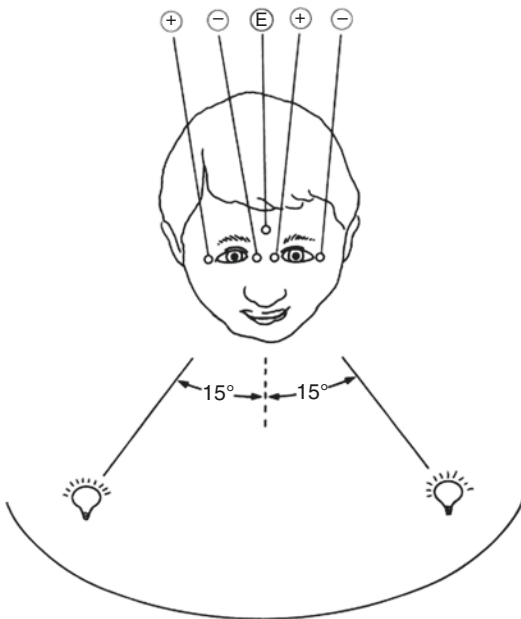


Fig. 19.15 Principle of EOG method

examiner should check the patient's compliance and noise to ensure proper recording during the test. Light adaptation is done with 100 cd/m². If the patient complains of severe glare, the light intensity increases gradually for 20 s. EOG is recorded every 1 min for 15 min. At each recorded time point, the magnitude of the amplitude is continuously plotted on the vertical line, and the time (min) is plotted on the transverse line. Then EOG period curve is created. Some irregular amplitude can be recorded due to noise; it is roughly drawn with a smooth curve passing through the middle of each point. Experienced examiner can manually draw or can be drawn automatically by built-in program. Minimal amplitude of EOG after dark adaptation is called as dark trough; maximal amplitude of EOG after light adaptation is called as light peak (Fig. 19.16).

19.5.2 Interpretation

Normally there is a transient increase in amplitude after dark adaptation and then it decreases with time. It is lowest at around 10 min after dark adaptation and slightly increases afterwards. The ratio of light peak by dark trough is called as Arden ratio. The Arden ratio value with 2.0 or more is normal, 2.0–1.5 is subnormal, and 1.5 or less is abnormal (Fig. 19.17).

19.6 Ocular Electromyography, EMG

Ocular motor nerve palsy which causes eye movement disorder and neuromuscular junction disorder is all targeted. Ocular electromyography (EMG) is used for monitoring when injecting botulinum toxin into the external ocular muscle for strabismus treatment.

EMG is finding, amplifying, and recording of electrical activity within the muscle. However, its clinical use is limited because the results are not easily quantified. Mean rectified voltage (MRV) is the average value obtained by rectifying alternating current and converting it into direct current. It is a quantitative measure of

Fig. 19.16 Waveform of EOG (ISCEV standard, 2010 update)

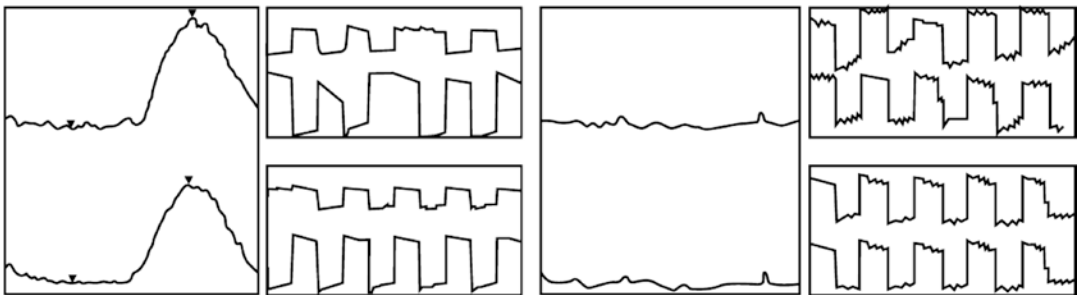
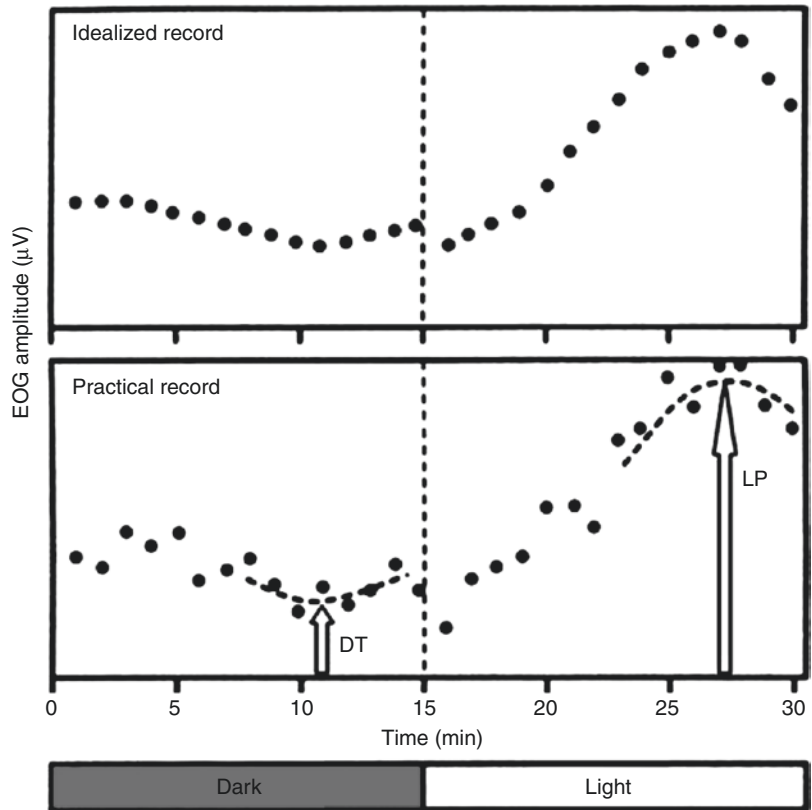


Fig. 19.17 Arden ratio of EOG. Normal (●: 2.0) and Best disease (▲: 1.3)

EMG. Root mean square (RMS) is electric current or electric value which has an AC waveform that is expressed by RMS value using the formula. It is compared to the tension of the external ocular muscle.

19.6.1 Method

The neutral electrode and the ground electrode are first contacted with the skin around the eyes. A very thin electrode is inserted through the

conjunctiva into the muscle under local anesthesia. The position of the electrode is adjusted until appropriate electrical activity appears. Normally, electrical activity is maximized when moving in the direction of muscle motion, and electrical activity is minimal when moving in the opposite direction.

19.7 Electronystagmography, ENG

Electronystagmography (ENG) is recording of eyeball movement using EOG. It is used in the diagnosis and treatment of various eye movement disorders. It is more sensitive than direct eyeball observation in patients with nystagmus and helps to distinguish the type of nystagmus by recording the movements quantitatively and calculating the velocity of eyeball movements.

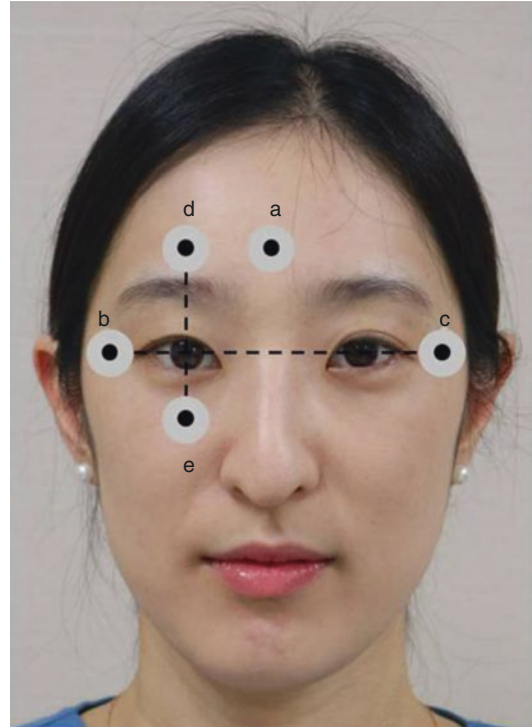
19.7.1 Method

19.7.1.1 Examination of Nystagmus

The method of attaching the electrodes may be the same as EOG, or each electrode may be attached to the skin of the lateral canthal area of both eyes. For measuring vertical movement, electrodes are attached to the upper and lower eyelids (Fig. 19.18). The degree of nystagmus is recorded in patient with nystagmus. According to patient's symptoms, saccadic movement and pursuit movement are induced using target or vestibulo-ocular reflex which is induced by rotation of patient's head, and then degree of nystagmus is recorded. Latent nystagmus is recorded with occluding one eye.

19.7.1.2 Examination of Eyeball Movement

The range of moving the target is within 20° left and right side and 30° in total. The recording



a. Reference electrode: frontal head
b,c. Horizontal movements: medial, lateral canthus
d,e. Vertical movements: upper, lower lids

Fig. 19.18 Electrode attachment site of ENG

electrode uses a silver electrode for EEG. The connecting line of both electrodes is placed passing through the pupil center horizontally or vertically close to the eyeball in primary position. Initially, the recorder is operated while moving the target at a relatively high speed of about 0.3 Hz. A small vibration of high speed is recorded almost simultaneously as the target moves. The velocity of target in pursuit movement is 0.1 Hz, 0.2 Hz, and 0.3 Hz, and the saccadic movement is around 0.3 Hz. Each movement is recorded for 30 s at a recording paper speed of about 10 mm/s. When the motor eyeball movement abnormality is suspected, the recording paper is accelerated at a speed of

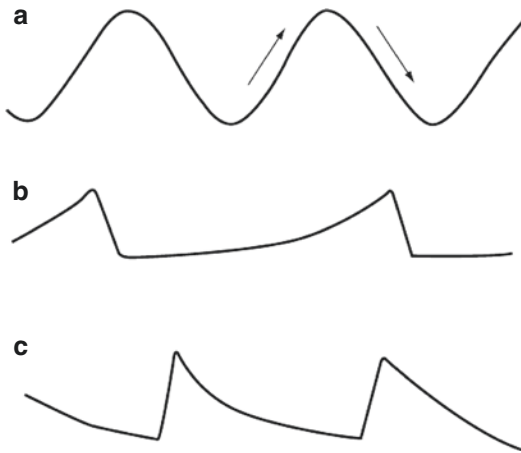


Fig. 19.19 Type of nystagmus: (a) pendular type, oscillations of equal velocity in each direction without the distinction between low speed and high speed; (b) accelerated type, the speed of eye movements increased at low speed; (c) decelerated type, the speed of eye movements decreased at low speed

50–100 mm/s and the target is reciprocated about 10 times.

The right motion is recorded upward and the left motion is recorded downward. It can be classified into several types depending on the type of nystagmus (Fig. 19.19).

Suggested Reading

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