Review Article

OCULAR ELECTRODIAGNOSIS

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INTRODUCTION

As we know every cell in the body exhibits electrical potential which is modified either by the cell activity itself or by a stimulus acting on the cell. These changes can be measured either by placing electrodes on the organ itself or at a remote place.

The changes in the electrical potentials produced by sensory stimulation are called 'evoked responses'. In eye there are three types of evoked potentials i.e. Electroretinogram (ERG), Electroculogram (EOG) and Visually evoked potentials (VEP).

Emil DuBois Reymond, Professor of physiology in Berlin was the first to describe the difference in potentials between the cornea and posterior pole of the eye in 1849.[1] Holmgren in 1865 showed that this resting potential can be modified by shining light on the eye.[2] Dewar and McKendrick unaware of Holmgren work published their work in 1873.[3] They carried out extensive experiments, initially placing the electrodes on the cornea and posterior pole of the eye. Later they were able to measure the potentials by placing the electrodes on the cornea and adjusent skin. But these early attempts in performing human ERG were very exhausting and far from satisfactory.

These potentials are very small and difficult to measure, but recent advances in electronics and computer assisted averaging techniques has made it possible to measure it more accurately, and has made the electrodiagnostic test a worthwhile clinical routine.

Electroretinogram (ERG)

The normal resting potential difference between the cornea and posterior pole which is about 1 mV is modified by a brief flash of light. To measure this a positive electrode is placed on the cornea embedded in a contact lens, a reference electrode is attached to the ear lobe and an earth electrode is placed on the forehead. We measure the average response of 64 flashes (Fig. 1).

The normal ERG has a small negative a-wave generated by inner segments of the rods and cones, followed by a large b-wave generated by Muller cells and bipolar cells. The wavelets on the b-wave are believed to be arising from inner retina and are abolished in ischaemia of the retina from central retinal artery occlusion and severe diabetic retinopathy. If we use a sufficiently strong flash and a fast recording apparatus we can also demonstrate another component of the ERG called Early Receptor Potential (ERP) believed to be arising from outer segments of rods and cones (Fig. 2, 3).

We must remember that a flash ERG is a mass retinal response and a small focal

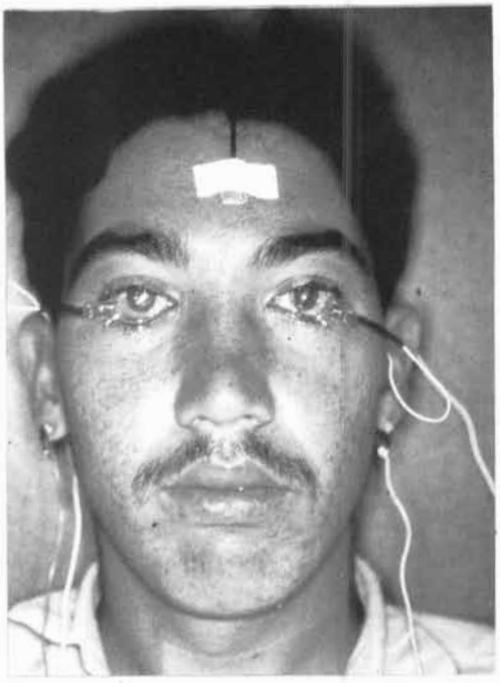

Fig. 1. Placement of electrodes for ERG.

lesion like senile macular degeneration will not be shown onroutine ERG. ERG can also be normal in the presence of optic atrophy from ganglion cells damage.

Electroocoulogram (EOG)

When the eyes are exposed to constant illumination after a period of darkness, the corneo-retinal potentials shows slow rises and falls over a period of hours. The

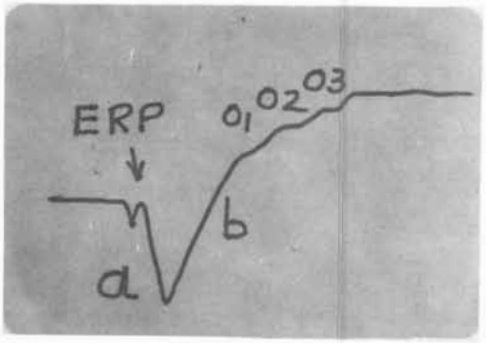

Fig. 2. Various components of a normal ERG.

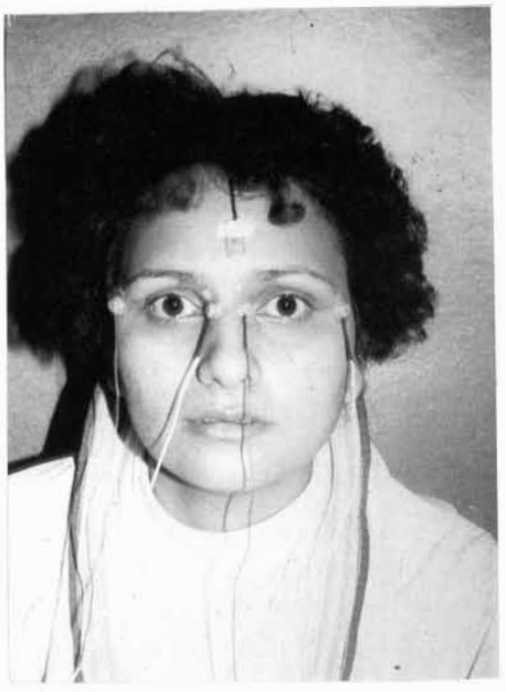

Fig. 4. Placement of electrodes for EOG.

measurements of this initial fall in darkness and subsequent rise in light is the basis of this test.

The electrodes are attached to the skin of the lateral and medial canthi in such a way that the electrodes on the right side of the eyes are connected to the positive terminal while electrodes on the left side of the eyes are connected to the negative terminal of the machine (Fig 4). The patient is instructed to look to the right and left alternatively following the movements of the light. When he looks to the right the electrodes on the right side of the eyes register a positive potential and there is an upward deflection of the recording pen. When the patient looks to the left the electrodes on the left side of the eyes register a positive potential and there is a downward deflection of the recording pen. The test is first carried out in the dark for a period of 12.50 minutes. during this time there is gradual reduction of the deflection. The lights are then put on and the test is

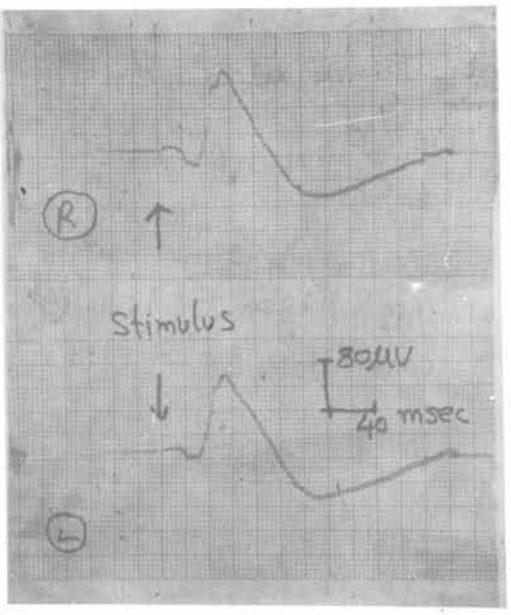

Fig. 3. Normal ERG from right and left eyes generated by Pantop M2 machine.

continued for another 12.50 minutes. During this time there is gradual increase in the deflection which levels of after about 7 minutes. The ratio between the highest reading in the light and lowest reading in the dark is calculated which is called Arden index. In the normal subjects it is between 2.5 and 3.0 (Fig. 5).

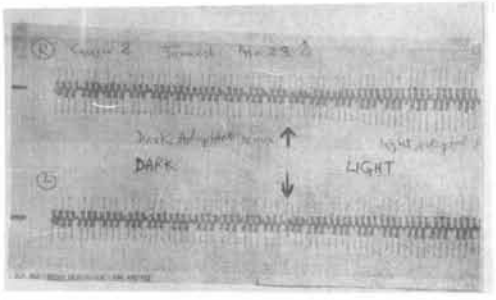

Fig. 5. Normal EOG response.

Visually evoked potentials (VEP)

The changes evoked by visual stimuli were first recorded in animals directly from the surface of pia matter by Fisher in 1930.[4] The introduction of computer assisted signal averaging of a large number of responses has made it possible to measure these small electrical changes more accurately. It also eliminates the unwanted background noise.

The active electrodes are placed in the occipital area, about 2 cms on either side and 2 cms above the occipital bump. We use subcutaneous which are easy to apply and give better results. The reference electrode is attached to the earlobe. The patient is also earthed by placing an electrode to the middle of the forehead.

The VEP recording is carried out on the two occipital zones by means of monocular stimulation. This examination can be carried out both with flash or checkboard stimulation (Fig. 6).

The stimulus we normally use is a pattern reversal black and white squares on a TV monitor. Each square subtends an angle of 20 degrees. The patterns are reversed at a frequency of 2 Hz and 96 times. Each eye is tested separately. The responses of 96 stimuli is averaged in the machine and is recorded on a paper.

The characteristics of a normal VEP depends upon the type of stimulus being

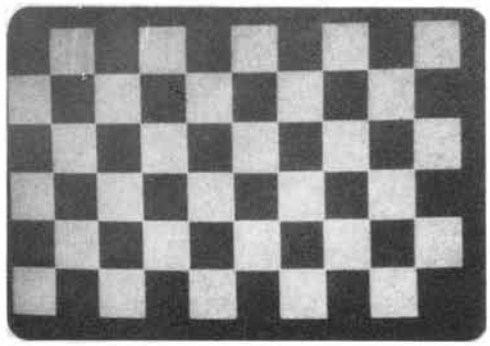

Fig. 6. Check stimulus used for VER.

used and the position of scalp electrodes. It also varies from one individual to another. Generally three peaks can be identified; a positive peak at about 70-100 ms, a negative at about 100-120 ms and a second positive at about 150 ms (Fig. 7).

The latency of the response is increased in retrobulbar neuritis, which remains high even after complete recovery. This may be the only evidence of a previous attack.

The VEP may be used in children to assess the visual acuity objectively by gradually reducing the size of the squares. The response falls sharply when the squares are no longer discernible. VEP may also be helpful in monitoring the function of optic nerve during orbital surgery and assessing damage to the optic nerve following head injury.

A. Factors influencing normal electroretinogram

Physiological variations

1. The effect of dark adaptation

During dark adapted state the b-wave increases in size and changes it's shape by becoming more round.

2. The effect of pupil size.

The size of b-wave increases in size with increase in the size of pupil.

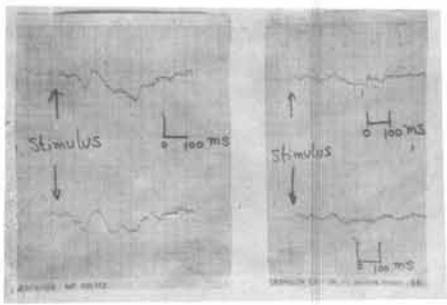

Fig. 7. VER from a normal person (left) and a patient with Optic neuritis (right).

3. The effect of age and sex

ERG can be recorded within a few hours after birth if a strong stimulus is used. It reaches it's adult size at the age of two years. After the age of two years it starts declining. ERG is slightly larger in women than in men.

4. The nature of stimulus

The amplitude of b-wave gradually increases in size with the increasing intensity of stimulus in dark adapted state. When it reaches it's maximum size , then it starts declining.

If a flickering light stimulus is used with a frequency of 30 Hz, the resulting ERG is thought to arise mainly from cones, as rods do not function at this frequency.

5. The effect of refractive errors

Both myopes and hypermetropes show a lower b-wave potentials than persons with no refractive errors.

6. The effect on response

ERG is a response from retinal receptors and bipolar cell. Blindness either by ganglion cell damage or by optic nerve damage will show a normal ERG. In macular degeneration ERG is also normal. A normal ERG is also elicited in the presence of dense opacities in the media.

B. Hereditary retinal diseases (HRD)

It is a group of diseases which have a hereditary tendency. A common feature is the presence of pigment migrated from retinal pigment epithelium (RPE). It represent a significant cause of blindness. Over 100,000 people are affected in USA. Many HRD can now be diagnosed early in life base on defective visual functions, defect in evoked potentials, biochemical abnormalities and molecular genetic defects much before any symptoms and signs develop. The capacity to diagnose these conditions at an

early stage gives us the hope that some of these diseases may be reversed, stabilised or slowed down.

1. Retinitis pigmentosa (RP)

Retinitis pigmentosa was first diagnosed by Donders in 1855 soon after the invention of ophthalmoscope.[5] It's prevalence is 1 in 4000 worldwide. In a study in USA the percentage of various genetic types were as follows: Autosomal dominant 19%, autosomal recessive 19%, X-linked 8%, undetermined 8% and isolates 40%.[6]

Clinically RP is characterised by night blindness, waxy pale disk, narrow vessels, bony spicule pigmentation at equatorial region, subcapsular lenticular opacities and cystoid macular oedema.

Karpe in 1945 discovered that patients with advanced RP had very small or non detectable ERGs.[7] It has now been shown that ERG changes could be detected in some cases years before diagnostic changes

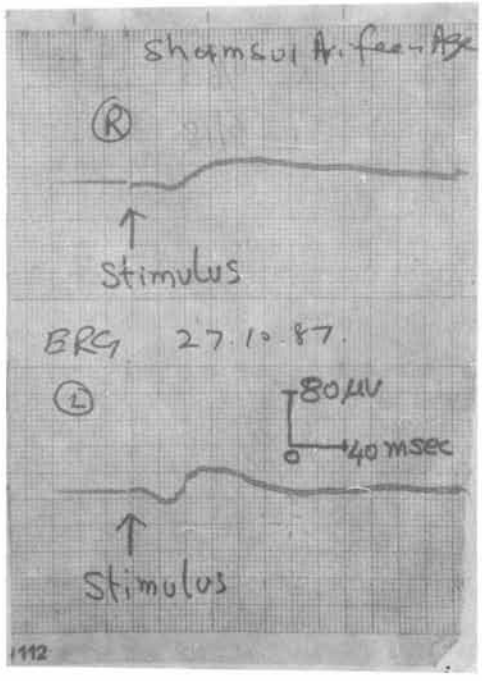

Fig. 8. ERG from a patient with RP.

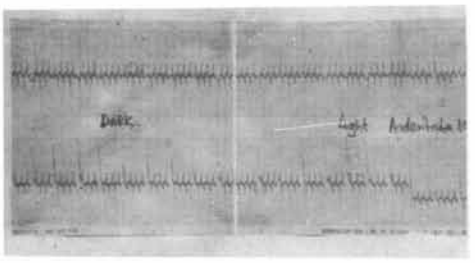

Fig. 9. EOG from a patient with RP showing no light rise.

are visible on fundus examination. The response to a white flash is reduced in all genetic types of RP (Fig. 8, 9). The subnormal or extinguished response seen in progressive type of RP contrasts with subnormal response in self limited form of sector RP.

Relatives of RP patients of age 6 and above with normal ERG responses are nor known to have developed this disease at a later life.[8,9]

Female carriers of X-linked RP may show a patch of bone spicule pigmentation with abnormal tapetal macular reflex. ERG in 90% of obligate carriers show reduced amplitude. Daughters of obligate carriers show either normal ERG or that similar to obligate carriers. Once a female carriers of X-linked type is detected on fundoscopy or ERG, she will have 50% chance of having an affected son or carrier daughter. Some female carriers of X-linked type may show considerable reduction in ERG.

Female carriers of autosomal recessive RP have normal fundi and normal ERG.

2. Abetalipoproteinaemia (Bassen-Kornzweig syndrome)

It is an autosomal recessive condition characterised by features of RP, ataxia, acanthocytosis, low serum cholesterol, and triglycerides. Patients have deficiency of vitamin A, E and K. Large doses of

vitamin A have resulted in return of normal dark adaptation threshold and normal ERG response in the early stage of the disease.[10] More advanced cases have not responded to the therapy. Vitamin E has been advocated to prevent the progression of this retinal degenration.

3. Refsum's disease

It is an inborn error of metabolism characterised by RP, ataxia, peripheral neuropathy, increased CSF protein and high serum phytanic acid levels. ERG is typical of RP.[11] Treatment consists of restriction of dairy products and green leafy vegetables. Body weight should also be maintained, as reduced body weight releases phytanic acid from tissue stores.

4. Leber's congenital amaurosis

It is an autosomal recessive disorder associated with sever visual loss, nystagmus and markedly reduced ERG.[12] Fundus shows white dots with bony spicule pigmentation. Parents would know that they have 25% chance of having affected child on subsequent deliveries.

5. Retinitis punctata albescence

An autosomal recessive disorder associated with signs and symptoms of RP. Fundi shows multiple white dots at the level of RPE. ERG is invariably abnormal.

6. Choroideraemia

It is an X-linked inherited disorder. In early stage visual acuity (VA) is normal with slight increase in dark adaptation threshold. Fundus shows granularity and depigmentation of RPE. ERG is reduced.

In more advanced cases there is marked reduction in VA, with increased dark adaptation threshold, restriction of visual fields and extensive choroidal atrophy. ERG is non detectable.

Obligate female carriers shows patchy depigmentation of RPE. However, they have normal VA, dark adaptation threshold and normal ERG.[13]

7. Gyrate atrophy

This disorder is due to deficiency of ornithine keto-acid aminotransferase. They have myopia, restricted visual fields, and elevated dark adaptation threshold. Fundi shows well demarcated chorioretinal atrophic patches in the periphery. ERG is non detectable.[14] There is elevation of plasma ornithine, hypolysinaemia and hyperornithinuria. Treatment consists of high doses of vitamin B6 and low protein and arginine diet.

8. Stationary night blindness

It is normal or nearly normal cone response with full field ERG that separates all these form of night blindness from all forms of night blindness associated with early stages of RP.

a. Congenital stationary night blindness (CSNB) with myopia.

It is inherited either as X-linked or autosomal recessive.[15] Myopia is between 3.5D and 14.5D. There is nondetectable rod ERG but normal cone response. Light rise in EOG is normal.

The ERG abnormality in CSNB with myopia has been reported as an acquired defect in patients with cutaneous malignant melanoma. The development of an antibody to melanoma reacts with retinal cells, thus interrupts rod transmission.[16]

b. Fundus albipunctatus

It is an autosomal recessive disorder. There is defect in the visual pigment regeneration. Fundus shows white deposits in midperiphery. After full dark adaptation ERG is normal.

c. Oguchi's disease

It is also an autosomal recessive disorder. Fundus exhibits characteristic change of colour from golden-brown in light

adapted state to normal colour in dark adapted state (Mizuo phenomenon). After one hour dark adaptation there is no rod response while cone response is normal. After complete dark adaptation some patients show normal rod response but only to one or two flashes. The light rise of EOG is preserved.

C. Hereditary macular diseases

It constitutes a significant cause of visual loss in children and young adults. It usually progresses to legal blindness. It hampers learning at school and interfere with occupational performance. Many of these children are extremely photophobic.

1. Vitelliform macular dystrophy (Best's disease)

It is an autosomal dominant disorder. It passes through 4 stages.[17,18] Previtelliform stage has normal fundus appearance with normal VA. Vitelliform stage is characterised by appearance of a round yellow lesion at the macula. Vision may be slightly affected. The yellow lesion can break through RPE and accumulate in the subretinal space inferiorly giving pseudohypopyon appearance. A scramble egg appearance appear when the yellow material scatters through the posterior fundus. EOG is affected while ERG is normal.[19,20]

2. Stargardt's disease (Fundus flavimaculatus)

It is an autosomal recessive disease. It is characterised by appearance of yellow flecks at the level of RPE at the posterior pole. These flecks either don't fluoresce or show irregular fluorescence. ERG is normal whereas EOG is abnormal.

D. Acquired Retinal Diseases

1. Retinal detachment

The amplitude of b-wave is reduced. The reduction depends upon the extent of detachment. After successful reattachment surgery b-wave recovers but the recovery lags behind the visual recovery. As ERG can be recorded in the presence of dense opacities in the media, a good response will be consistent with absence of disease.

2. Diabetic retinopathy

There is selective abolition of oscillatory potentials in patients with diabetic retinopathy. The loss of these wavelets suggests ischaemia, as they are also lost in other vascular occlusive diseases.[21]

3. Vascular occlusion

ERG is sensitive to retinal vascular diseases. In central retinal artery occlusion there is loss of oscillatory potentials independent of a-wave and slight diminution of b-wave.

In central retinal vein occlusion the changes are similar in nature.[22]

4. Drugs

Certain drugs like chloroquine are stored in retinal pigment epithelium. It's toxic effects may be seen in EOG and ERG before clinical effect are evident.

5. Trauma

In contusion injuries there is abolition of ERG. However, it soon starts recovering.

Similarly after perforating injury the response is abolished due to short circuiting. As the wound heals, the response starts recovering.

6. Ocular metallosis

Specific changes occurs in siderosis. Initially there is increase in a-wave called negative plus and later there is decrease in b-wave called negative minus.[23]

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