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EDITORIAL

Electroretinography - An Evolving Technique for Early Detection of Retinal Dysfunction

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Human vision comprises different structures whose physiological functions act as variable for a healthy human vision. Retina plays a vital role in vision, in hosting different cells and neuron in ten layers. The perikaryal of these neurons are segregated from neurological processes, forming discrete layers[1]. The inner retina includes ganglion cells and amacrine cells, whereas the outer retina includes the rod and cone photoreceptors. The primary role of photoreceptors is to convert light energy into an electrical signal (phototransduction)[2]. The photoreceptors transmit visual information to second-order neurons known as bipolar cells in the middle retina. Rods synapse only with depolarizing bipolar cells, while cones synapse with both depolarizing and hyperpolarizing bipolar cells[3]. Electrophysiological responses from these cells can be recorded for testing of different diseases by using a technique known as "Electroretinography (ERG)". This editorial explains how ERG can be used for testing dysfunctions, dystrophies, and the early detection of glaucoma.

Introduction to ERG: ERG is like "Electrocardiography (ECG)" in the fashion that electrodes are used to measure the electrical activity in both techniques. In ERG, electrodes are placed below the eye, which are measuring the electrical response of retinal cells. Every type of cell responds differently to light intensities and frequencies, which is why ERG can detect the exact part of the retina which is not functioning properly. Photoreceptors respond to flashes with a frequency between 2-4 Hz. Bipolar cells respond to flicker (bright white light) with a frequency of 28.3. Ganglion cells will respond to red flashed with blue background with a particular number of flashes (100 flashed as per ISO). By projecting the light, the best suitable manner, like flickering and flashing, the activities of retinal cells are recorded in a wave-like output[4].

Components of Waveform: The output wave consists of three different waves because the ERG hits three different types of cells and their responses are measured accordingly. These waves are as follows.

A-wave is generated by the photoreceptors (rods and cones) as these are the first to receive the light. Abnormalities in the outer retina are detected by the abnormalities in the a-wave.

B-wave is generated because of the response from the bipolar cells of the retina. Bipolar cells are second to receive the light, and inner retinal photoconduction is tested by this wave. Light goes to the ganglion cells afterward.

PhNR wave which is the function of the response of the innermost retinal cell layer and is used for the early detection of glaucoma and optic nerve dystrophies[2].

Analysis of Results

Amplitude: The amplitude is the maximal light-induced electrical response (voltage) generated by the various retinal cells[2]. It indicates that a substantial number of retinal cells are present, however, the abnormal, usually low amplitude indicates that the number of cells is decreasing cells, and retinal cells are dying. A baseline is present, and the measurement of a-wave is taken from baseline to the minima in a negative cycle, the same as the q-wave of EKG. B-wave amplitude is measured from the negative peak of A-wave to the B-wave peak. The amplitude of PhNR is measured from the baseline of the ERG to the negative peak of the PhNR[3].

Implicit Time: Implicit time (time-to-peak) refers to the time needed for the electrical response to reach maximum amplitude. The normal implicit time, also regarded as the latent or peak time, indicates the healthy metabolic activity of the retinal cells, whereas abnormality in the implicit time is an indicator of the below-average performance of the retinal cells[2]. These discrepancies are seen as the function of their amplitude (μV) and the implicit time (ms). A discrepancy in A-wave will direct the physician to dystrophies and degenerations in the retina and B-wave discrepancies direct physicians to the micro-vascularization of the retina, like diabetic retinopathy, central retinal vein occlusion, etc. After bipolar cells, light goes to ganglion cells which make the optic nerve. PhNR is a test used for the early detection of glaucoma and optic nerve dystrophies. Similarly, normal PhNR wave shows the proper functioning of the ganglion and glial cells, and abnormality in their amplitude and peak time indicate altered or reduced cells performance of retinal and glial cells[3].

Current Screening Tools and ERG: There are between 90-120 million cells present on Retina, and currently, their health is accessed through the analysis of vasculature above them (fundus exam) and a highly mathematically influenced OCT/angio-OCT scan. Other Currently available retinal testing tools are perimetry, fundus imaging, and tonometry. ERG is an objective functional test that measures the response of right now without being affected by either the patient or the person performing the test. How ERG has potential advantages over all these techniques is explained below[4].

OCT/Angio OCT and Fundus Imaging: OCT is a highly mathematically influenced testing technique, it shows the decreased number of cells in the retina, and these exams provide a method of assessing the cellular organization and axonal thickness in glaucoma, showing the optic nerve head, Disc rim, Cup to Disk ratio and RNFL thickness. But there are limitations to these tests courtesy of the large differences in the normal optic disk and peripapillary region morphology, and high signal strength is needed to perform these tests. Artifacts also come to play. The other drawback is that it only shows the decreased number of cells, while these cells can be long dead, or still dying. No information is provided in such regard. mid fundus imaging system offers only a light sensitivity of around 72%. OCT and Angio OCT are expensive to acquire and required the supervision of professionals. Their results are AI analyzed which is a problem because they can only analyze gradable images, while in real-life, one out of three images is non-gradable. These imaging modalities do not represent any of the cellular response, but only present a scanned picture of the area being captured. It cannot be told from watching the pictures if the cells are performing normally or not. In most patients, diabetic retinopathy is diagnosed too late. ERG gives an advantage over OCTs as the health of cells and their performance can easily be measured with ERG[5].

Tonometry: Intraocular pressure gives information about the fluid pressure in the eye. This test is easy and non-invasive mostly, but there are limitations that normal-tension glaucoma goes undetected by this. Sometimes, hypertension is considered glaucoma because hypertension can cause high IOP. You can have high IOP without glaucoma and you can have glaucoma with low IOP too. With ERG, one might not be able to know the IOP, but it can easily be told that whether cells are dying or not. Furthermore, the high IOP can be verified whether it came out of glaucoma or some other reason. Similarly, low IOP glaucoma can be verified too. One just has to perform the test and examine the readings[6].

Perimetry: It is a visual field test that has an ability to determine central or peripheral vision loss affected by a combination of

medical disorders, including glaucoma. Its limitations are that these tests are highly variable and require a lot of patient input, which can be a real problem when dealing with kids and patients with old age. This test doesn't give an evident response either until at least 30% of the ganglion cells have been damaged. This test too represents not the cellular response but a field in which the patient can see. Perimetry tests take usually more than ten minutes to complete which can be a problem when working with old patients. With ERG, testing to detect glaucoma can be done in a much shorter time, and ERG does not require patient input too. ERG is not affected by the actions or input the patient performs[7].

Limitations of ERG: ERG can measure 96% of patients, lacks 4% due to issues like pupil can't be dilated, vitreous and focus issues, and structural anomalies. Furthermore, two types of patients require prior medication before ERG testing. Ones are the patients with photosensitive epilepsy because a high frequency of flicker can induce epilepsy seizures. The second type of patient is the ones with pharmacological migraines. Subjects with nystagmus require to be dilated[3].

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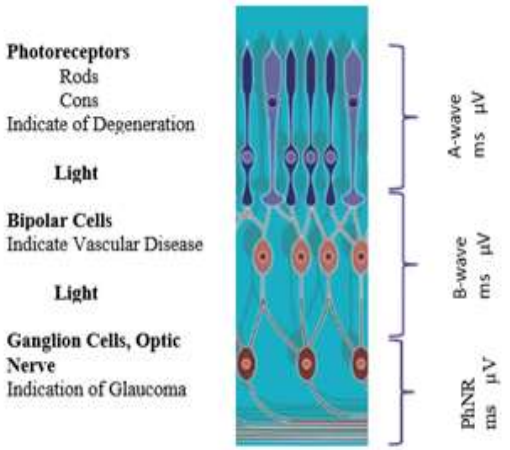

Figure 1: Order of ERG wave formation

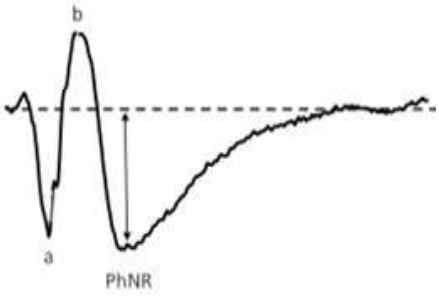

Figure 2: A normal ERG Wave Source: Samuel A; Rustum K. Full field Electroretinogram