THE ELECTRICAL CHANGES IN THE RETINA

THESIS

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بسم الله الرحمن الرحيم

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THE ELECTRORETINOGRAM
(ERG)

THE ELECTRORETINOGRAM

Introduction

The study of electrical changes in the eye has now been in progress for more than a hundred years, and electrophysiological measurements on the eye are now becoming part of our clinical routine. In the early years these studies were largely confined to experimental animals, but there is now an international society of clinical electroretinography which has been in existence for over 15 years. The first work in this field was concerned with the corneo-retinal potential, or the resting potential. This may be defined as the difference in potential between the cornea and the posterior pole of the eye. It was first described by Emil DuBois Reymond, professor of physiology in Berlin (DuBois Reymond, 1849). He showed that the cornea is electrically positive with respect to the posterior pole; however, it was not until 16 years later that Holmgren observed that the resting potential can be modified by the action of light shining on the retina (Holmgren 1865). Shortly after this Dewar and Mckendrick, working in Edinburgh, rediscovered this light response quite independently and they came upon Holmgren's paper after their own results had been published (Dewar and Mckendrick, 1893). They were able to show that the changes in potential on impact of light amounted to three to ten percent of the normal resting potential and that they were independent of the anterior portion of the eye: Initially their experiments were carried out by placing electrodes on the cornea and the posterior pole of the eye, but they subsequently showed that the response to light could also be recorded between the exposed brain and the cornea allowing the eye to be left in situ. They then found that the same electrical changes could be recorded by placing electrodes on the cornea and an adjacent area of skin. Having made this discovery they were able to attempt to produce a human electroretinogram. (Galloway 1975).

THE EVOLUTION OF ELECTRORETINOGRAPHY

At the turn of the century considerable advances were made in the techniques of recording electrical responses in animals. In 1903 Gotch. working in the physiological laboratory at oxford, recorded responses from excised frogs'eyes. He was able to photograph his records and he found that the positive component of the electroretinogram measured up to 0.001 V and was preceded by a slight dip of negativity (Gotch, 1903). It was known therefore at the turn of the century that a biphasic type of response could be produced by a single flash of light. In 1908 Einthoven and Jolly showed the presence of a third and later component in the electroretinogram, the positive 'C' wave. The negative and positive waves preceeding this have been known as the 'a' and 'b' waves respectively (Einthoven and Jolly, 1908). The introduction of the valve amplifier brought about a dramatic improvement in recording techniques and led to a further understanding of the origin and nature of the response. In 1925 Hartline carried out a series of detailed experiments confirming that the response from intact animals was identical to that obtained from excised open eyes (Hartline 1925). In the early 1930s, attempts were being made to record the human electroretinogram using the valve amplifier, but at the same time an important milestone was reached in the study of responses from animals. This was the classical work of Granit on cats. He developed the ideas put forward by Einthoven and Jolly after the turn of the century, suggesting that the electroretinogram represents the sum of three waveforms which he termed "processes". These he enumerated as P I; P II and P III. He showed that if the electroretinogram is recorded from a cat which is subjected to deepening levels of ether anaesthesia, then the waveform changes is a characteristic manner. This change in waveform was thought to be due to the selective inhibition of the three processes, P I; P II and P III in turn. Although they have been elaborated to some extent, these original ideas about the nature of the electroretinogram are still held to be true today (Granit 1933). As soon as the Knowledge of the basic components had become well established, much interest was centered on the relative contribution of photopic and scotopic mechanisms to the response.

Although it can be seen that considerable advances were being made in our understanding of the electrical responses from the eye from work on animals, investigaions on human subjects had always been hampered by the technical problem of fixing the electrodes. However, a great step forward was made in 1941 when Riggs introduced the contact lens electrode. Infact the use of the contact lens remained in abeyance during the war years until the pioneering work of karpe began to be published from Stockholm in 1945.

using the method described by karpe, the human electroretinogram could be recorded as a biphasic response, a negative 'a' wave followed by a positive 'b' wave the 'C' wave was not usually seen due to the brief duration of the stimulus. But it had been previously shown in other animals that a series of small wavelets could be sometimes seen on the 'b' wave (Frohlich 1914; Granit 1947). In 1954 Cobb and Morton described the phenomenon in man and named it the Oscillatory Potential. The most recent component of importance to be discovered is the Early Receptor Potential. This is a very rapid component which can be seen at the very begining of the response immediately before the 'a' wave. Brown and Murakami first described it in(1964) and showed that it could only be elicited by an intense light stimulus.

Until recently the routine method of recording the E.R.G. entailed enlarging or amplifying the minute electrical changes picked up from corneal and skin electrodes and reproducing them on paper by some form of penwriter. However, the use of the oscilloscope as a recording instrument now gives a more accurate response and the result can be photographed with polaroid film. Afurther advance has been the introduction of the technique of averaging. Signal averaging is a valuable way of separating the true response from background interference. The method involves recording a series of consecutive responses from which an average trace is obtained. The crudest way of doing this is simply to superimpose these repeated responses using a pen recorder, but a more sophisticated and more useful method entails feeding the records into a computer which is programmed specifically for this purpose (Galloway, 1975).

General notions concerning retinal electrophysiology:

The activity of even the most specialized cell is accompanied by several physico-chemical phenomena of which the electrical is the most easily demonstrated.

The production of electrical activity in the retina obeys the general rules of cell electrophysiology. In a living cell the electrical charge is different on both sides of the cell membrane this difference is called the resting membrane potential and is due to an ionic unbalance between the intracellular contents (higher K^+ concenta-tion) and extracellular fluid (higher Na^+ concentration).

An appropriate stimulation (such as light for the photoreceptors) abruptly changes the biophysical charac-teristics of the cell membrane separating the intracellular &

extracellular media. Depolarization is brought about by the influx of Na^+ into the cell and the efflux of K^+ and is manifested by an abrupt potential difference, recorded as a spike and known as the action potential.

Rods and cones obey the same laws as all other cells. By means of complex experiments based on synaptic organization and intracellular electrical activity in various conditions of stimulation, the physiological properties of the different retinal layers have been shown. These have been resumed by Dowling (1970):

a) The outer plexiform layer contributes to the static or spatial aspect of the illumination which excites the photoreceptors. The neurones which constitute this layer respond to stimulation by slow gradually changing and sustained potentials. As interactions between the neurone in the outer plexiform layer increase the contrast of the retinal image, they create an antagonistic organization between the stimulated center and the surrounding region (and Vice Versa) in the bipolar cells.

b) The inner plexiform layer contributes to the dynamic or temporal aspect of the illumination which excites the photoreceptors. The amacrine cells stress changes in retinal stimulation and respond especially to mobile stimuli. Interactions in the inner plexiform layer probably coutribute to the selective responses of the ganglion cells provided by movement and direction.

c) Both physiological types of ganglion cells in the vertebrate retina appear closely linked:

1. To bipolar cell activity and information concerning the transformations of the signal in the outer plexiform layer and.

2. To amacrine cell activity and information concerning the transformation of the signal in the inner plexiform layer. The role of the ganglion cells is to transmit these two types of information to the superior visual centers.

The initial mechanism for triggering off the electrobiogenesis in the photoreceptors is very complex, being mainly based on changes in membrane permeábility and the accompanying Na and K exchanges. The current to which the outer segment of photoreceptors gives rise is passively propagated towards the inner segment. In spite of its decay it is still capable of eliciting a photic sensation.

This brief and elementary introduction to the fundamental bioelectriecal phenomena of the retina is intended to show that the electrical activity as represented in the overall clinical ERG has a very complex origin. Interpretation of the ERG taken in context with the different pathologic conditions of the choroid and the retina has its limits and results can only be of a relative nature (Babel 1977).