Principles and Practice of Clinical Electrophysiology of Vision

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History of Electro-Oculography

Geoffrey B. Arden

The potential voltage difference that occurs between the cornea and fundus was known to DuBois-Reymond.[9] The main site of the voltage is across the retinal pigmented epithelium (RPE), and this was demonstrated by Dewar and M'Kendrick,[8] Kuhne and Steiner,[21] and de Haas[7]—all in the 19th century. Although illumination was known to affect the potential,[14, 21] the capillary electrometers used in early work were not sufficiently sensitive or stable to analyze the changes in detail. With the advent of electronic amplification, condenser coupling prevented recording the changes caused by light. It was not until the 1940s that Noell[38] was able to employ stable dc recording systems and follow the slow changes; he related the c-wave of the electroretinogram (ERG) to the later and still slower responses and related the effects of poisons such as iodate and azide to the morphological sites of action.

The eye movement potential was studied in humans by numerous authors, some of whom[6, 12, 19, 20, 29, 46] noted that the magnitude of the dipole was altered in illumination. The first complete description of the light-dark sequence was due to Kris,[19] but an analysis of the nature of the response and the recognition of its clinical utility is usually attributed to Arden.[1–4]

Since that time, research has moved along various lines; in animal work, the nature of the ionic channels and pumps in the apical and basal surfaces of the RPE has been greatly extended and related to water movement across the RPE. The most notable contributions are by Steinberg, Miller, Oakley, and other collaborators,* and the nature of the membrane changes that cause the c-wave, the "fast oscillation," and the light rise has been worked out in some detail. Further descriptions are given in the references in Chapters 8 to 10 and 39.

The pharmacology of the dc potential and its relation to neurotransmitters have recently been reinvestigated by several authors.[11, 24, 42, 47] The exact mechanisms of control still prove elusive, but this research has emphasized that interpretations from clinical work, especially the sensitivity to circulatory embarrassment,[5] are largely correct.

The eye movement potential in humans has also been frequently studied. It has been shown that cones contribute to the "light rise."[10] There have been attempts to describe the sequence of changes in terms of mathematical concepts (see Chapter 39), but this has not yet led to simplifications or to a reconciliation with cellular mechanisms. This is perhaps not surprising given that at least three separate mechanisms for current production have been identified in animal experiments, each with their own locations, while at each location, several different ionic mechanisms may be involved in current production.

Experimental clinical work has been more successful. This is covered in detail in Chapter 39. Recently, the relationship of ERG and electro-oculographic (EOG) changes in inflammatory disease has recently been analyzed,[18] although the major clinical use of the EOG is that a reduced EOG and normal

*13, 15–17, 23, 25, 26, 30–37, 39–41, 44, 45, and 48.

ERG are a diagnostic feature of Best's disease and some other forms of juvenile macular degeneration, as has been widely reported.[49] It is useful as an ancillary test in retinal degenerations and in cases of unexplained loss of vision. The influence of other agents on the EOG (mannitol and acetazolamide, a carbonic anhydrase inhibitor) has been studied by the Japanese school and clinical tests developed as a result.[27, 28, 50] Most recently, extension of this work has suggested that while acelazalamide acts directly on the membrane mechanisms, mannitol activates a "second messenger" system.[22]

Finally, continuing efforts have been made to reduce the population variability of the EOG as a clinical test. Some of these involve more lengthy periods of recording, but even if this results in greater precision, it is clinically difficult to justify. The original method envisaged a 12-minute period of dark adaptation followed by light adaptation for 10 minutes. The dark adaptation has been whittled down to "a period of reduced illumination sufficient to stabilize the voltage changes." In the author's experience, this sometimes takes as long as 60 minutes. Alternatively, more lengthy periods of dark adaptation have been suggested. Such modifications have their protagonists and are well described in Chapter 39. As yet unconfirmed on a large scale, a recent report[43] shows that part of the problem is due to errors in eye movement control. All eye movement techniques assume that the ocular excursions are precise, there is a linear relation between voltage and the degree of eye motion, and that the changes in recorded voltage are due only to changes in the apparent ocular dipole which generates the current. If the real ocular excursion is measured, and appropriate corrections made, variability decreases.

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