HANDBOOK OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

EDITOR-IN-CHIEF A. REMOND

VOLUME 8

Electrical Reactions of the Brain and Complementary Methods of Evaluation

EDITOR: P. BUSER

Faculty of Sciences, Paris (France)

PART B

Complementary Electrophysiological Techniques and Methods for Evaluation of the Central Nervous System

EDITOR: J. S. BARLOW

Massachusetts General Hospital, Boston, Mass. (U.S.A.)

ELSEVIER

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International Federation of Societies for EEG and Clinical Neurophysiology

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International Federation of Societies for EEG and Clinical Neurophysiology

A great need has long been felt for a Handbook giving a complete picture of the present-day knowledge on the electrical activity of the nervous system.

The International Federation of Societies for EEG and Clinical Neurophysiology is happy to be able to present such a Handbook, of which this is a small part.

The decision to prepare this work was made formally by the Federation at its VIIth International Congress. Since then nearly two hundred specialists from all over the world have collaborated in writing the Handbook, each part being prepared jointly by a team of writers.

The Handbook begins with an appraisal of 40 years of achievements by pioneers in these fields and an evaluation of the current use and future perspectives of EEG and EMG. The work subsequently progresses through a wide variety of topics—for example, an analysis of the basic principles of the electrogenesis of the nervous system; a critical review of techniques and methods, including data processing; a description of the normal EEG from birth to death, with special consideration of the effect of physiological and metabolic variables and of the changes relative to brain function and the individual's behaviour in his environment. Finally, a large clinical section covering the electrical abnormalities in various diseases is introduced by a study of electrographic semeiology and of the rules of diagnostic interpretation.

The Handbook will be published in 16 volumes comprising 40 parts (about 2500 pages altogether). For speed of publication most of the 40 parts will be published separately and in random order.

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PART B

COMPLEMENTARY ELECTROPHYSIOLOGICAL TECHNIQUES AND METHODS FOR EVALUATION OF THE CENTRAL NERVOUS SYSTEM

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G. H. M. van Lith, *Eye Hospital, Medical Faculty, Rotterdam (The Netherlands)*

Preface

Not infrequently it is desirable to use other methods to complement the electroencephalogram as a means of evaluation of the central nervous system. The following measures are considered in this discussion of complementary techniques: the electrooculogram, the electroretinogram (and the visual evoked response in relation to the latter), the electrodermogram, the electrocardiogram (as a monitor of heart rate), and measures of respiration. (The electromyogram is discussed in Volumes 2 and 16 of this Handbook; measures of peripheral nerve activity are also dealt with in the latter Volume.) The general problem of the quantitative comparison of electroencephalograms with recordings of any one of these measures, as a problem in data transformation, is also discussed; specific techniques for data processing are considered in Volumes 4 and 5.

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Section I. Introduction

The brain, by its very nature, always functions in relation to the rest of the body, as well as to the environment. It is hardly surprising, then, that in many instances it is desirable, even essential, to record one or more of those peripheral measures of activity elsewhere in the body which in turn reflect the activity or "state" of the brain itself, or are closely related to it.

To complement the electroencephalogram (EEG) as a direct method of evaluation of the brain, there are a number of peripheral measures that can be employed. Several of these can be considered as basically autonomic measures, *i.e.*, the electrocardiogram (EKG), the electrodermogram (EDG), measures of respiration. Others are referable to a particular organ; for example, the electroretinogram (ERG) and the electro-oculogram (EOG) are specifically related to the receptor and effector functions, respectively, of the eye. The electromyogram (EMG) and various types of measures of movement (*e.g.*, pressing a button or a telegraph key, or recording of movement by means of an accelerometer) are frequently employed as voluntary motor output measures of CNS function. Recording of the activity of peripheral nerves can also be considered as a complementary measure in relation to evaluation of CNS activity, particularly in those instances in which activity recorded from peripheral nerves provides a reference point, say, for CNS activity evoked by stimulation of peripheral nerves.

Quite often it may be desirable to record several complementary measures simultaneously, for example, the EKG and respiration, or the EKG and the EDG. These may be recorded together with the EEG, or without the latter. In studies of sleep, or of the orienting response, for example, several such measures may be recorded, *i.e.*, the EOG, the EDG, the EMG (from one or more muscles), the EKG, respiration, and some measure of bodily movement, all in addition to one or more channels of the EEG.

In specific instances, it may be that only some limited aspect of a given peripheral measure is of interest. For example, merely the AC component of the EOG may suffice in a given problem (for example, to monitor rapid eye movements during sleep). It is usually the case that only the heart or pulse rate (or their reciprocal, the interval between successive beats) is of interest, rather than the complete waveform of the EKG. The same may obtain for measures of respiration.

Save for the ERG, polygraphic recording is generally employed, sometimes with simultaneous recording onto magnetic tape, for subsequent automatic data-processing by means of a computer. Alternatively, the polygraphic data may be fed directly into a computer, for immediate or so-called on-line processing.

From the various possible complementary techniques that have been mentioned

above, the discussion in this Part will be limited to the EOG and ERG (see Section II) and to the following autonomic variables: electrodermal, cardiovascular (as reflected in heart rate), and respiratory (see Section III). Since nerve and muscle potentials are the subject of Volume 16, they will not be considered here. Mention may also be made of other works in this general area (*e.g.*, Brown 1967; Venables and Martin 1967a; Greenfield and Sternbach 1972).

For each of the peripheral measures under consideration, the nature and origin of the variable as well as recording techniques will be discussed. Especially for the autonomic variables, the dependence of the peripheral measures on the "state" of the central nervous system will be considered.

Particularly in view of the application of computer techniques to the analysis and evaluation of such data, some considerations will also be included concerning the problem of transformation of the data from various complementary measures and of the EEG itself so as to facilitate their mutual quantitative analysis (see Section IV).

Section II. Electrophysiology of the Visual System and Electrodiagnostic Procedures

A. INTRODUCTION

This survey is aimed at giving an insight into the electrodiagnostic procedures of the visual system. For better understanding, attention will also be paid to basic electrophysiology. A discussion of all the diseases in which electrodiagnostic procedures might prove valuable does not fall within the scope of this Section. Good surveys in this field are given by Jacobson (1961) and by Jayle *et al.* (1965). The published symposia of the ISCERG (International Society for Clinical Electroretinography) will provide more detailed descriptions of specific problems. In the context of this Handbook we will try to give an idea of the various measurable electrical responses of the visual system. Moreover, the relation between these responses and diseases of the eye is given by indicating the origin of the responses.

The following subjects will be dealt with: the electro-oculogram (EOG), the classical electroretinogram (ERG) with its four components a, b, c and d, the oscillatory potentials (OP), the early receptor potential (ERP), the local electroretinogram, also called the foveal ERG, and the visually evoked responses (VER); the latter will only be mentioned in connection with the ERG.

B. THE ELECTRO-OCULOGRAM (EOG)

The resting or standing potential of the eye has an even longer history than the ERG (Du Bois-Reymond 1849). It consists of a potential difference between the anterior and posterior pole of the eye.

1. *Recording procedure*

In human beings the standing potential can only be measured indirectly. Electrodes are placed on the skin over the orbital rim on either side of the eye (Fig. 1). Silver electrodes, normally used for the VER, can also serve for the EOG. Owing to its standing potential, the eye acts as an electric dipole. Because the cornea is positive in comparison with the back of the eye, eye movements to either side will manifest themselves as a positive voltage change at the electrodes towards which the cornea moves. When the electrodes are coupled to an AC amplifier with a long time constant (1–3 sec), looking regularly to left and right will result in the curve of Fig. 2,A, B. In this way involuntary eye movements can also be recorded, which is actually done in electronystagmography.

By standardizing the eye movements, *i.e.*, moving the eyes over a fixed angle to left

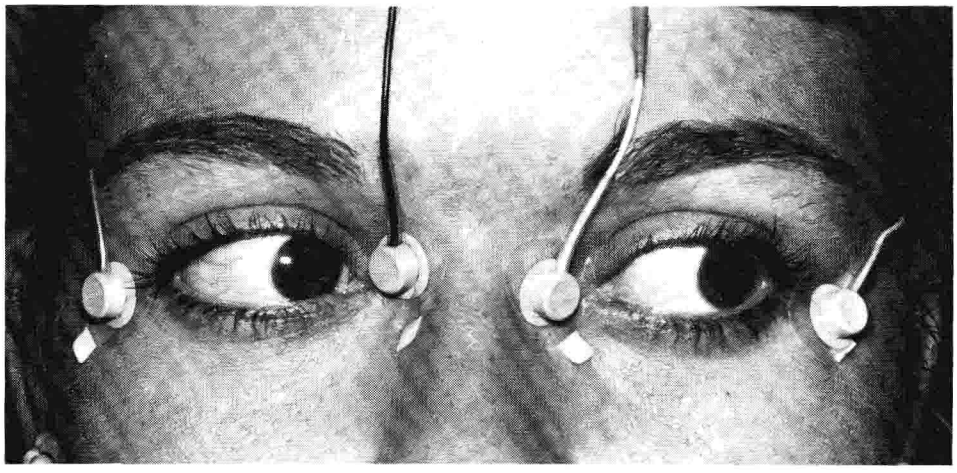

Fig. 1. Placement of the electrodes, nasally and temporally of the eye, for the recording of the (horizontal) electro-oculogram.

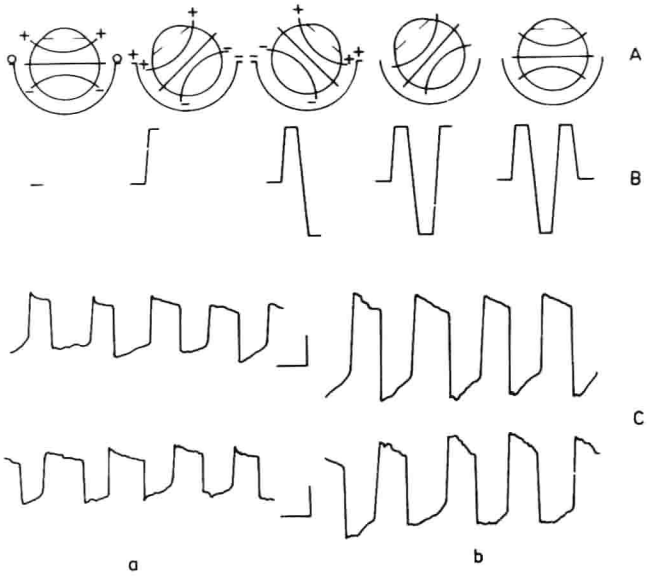

Fig. 2. (A) Alternating potentials at the electrodes when the eye is turned to the left and to the right. An upward deflection indicates movement of the eyes to the left. (B) Resulting curve when a dipole like the eye is turned to the left, to the right and to the left again. (C) Actual recording of the electro-oculogram, in the dark (a) and after light adaptation (b). Calibration: 500 μV, 500 msec. (Arden *et al.* 1962b)

and right, the height of the electrode deflections can also be used as a retinal function test (Fig. 2,C). Usually the eyes are moved over an angle of 30°, for which the deflections are about 100–200 μV. However, because this height is not only dependent on the height of the standing potential and the extent of the excursions of the eyes, but also on the resistance between skin and electrodes and on the position of the electrodes with respect to the globe, the interindividual variation is rather great (Arden and

Kelsey 1962c). This is why the indirect measurement of the standing potential itself is not utilized in electro-ophthalmology.

During light adaptation, and according to the luminance of the surroundings, the standing potential increases; this is the so-called light rise (Figs. 2 and 3). This light rise is not continuous, but transitory (Kris 1960); the maximum height is reached after about 10–15 min of light adaptation, after which period the standing potential decreases again until approximately the pre-light-adaptation value is reached. By measuring the light rise, and not the standing potential itself in absolute values, a useful clinical method has been developed (Arden *et al.* 1962b). These authors measured the ratio between the highest value in the light adapted state and the lowest value in the dark adapted state, the so-called light peak/dark trough-ratio (LP/DT ratio). With a light adaptation of about 20,000 trolands Arden *et al.* (1962b) found a mean ratio of about 2, while a lower limit for the normal retina of 1.85 could be established. A more precise differentiation (Van Lith and Balik 1970a) places the lower limit of normal at 1.65. It is clear that by applying the LP/DT-ratio, instead of

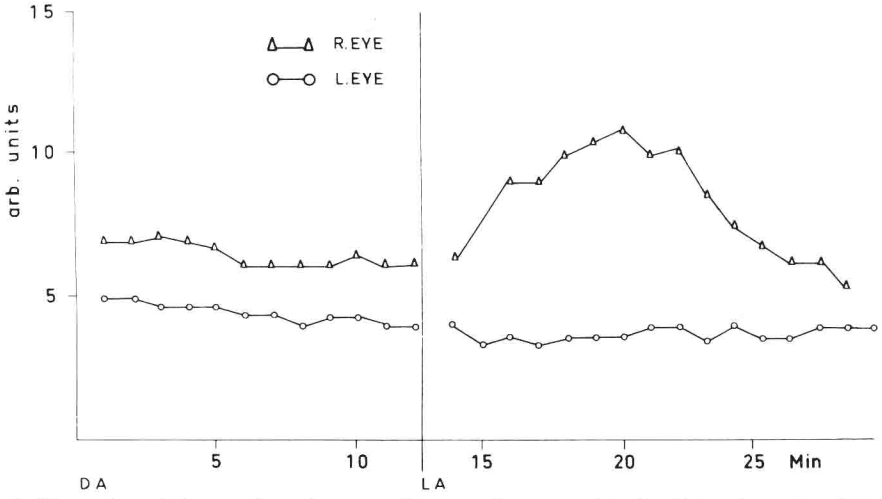

Fig. 3. Illustration of the transitory increase of the standing potential after light adaptation. DA, dark adaptation; LA, light adaptation. Right eye, normal curve. Left eye, no rise after light adaptation, due to a unilateral tapeto-retinal degeneration.

the standing potential itself, a number of factors which may cause great individual variations in the standing potential are diminished or eliminated (Arden and Barrada 1962a). Nevertheless, the ratio itself also appears to show considerable variations, both between individuals and in one and the same person (Kelsey 1967; Van Lith and Balik 1970a). If variations are taken into account, the determination of the LP/DT-ratio, for which the term EOG is also used, is a valuable tool for clinical work.

2. *Origin*

It is generally accepted that the origin of the standing potential is localized in the deep

retinal layers, probably in the pigment epithelium (Noell 1954, 1963; Brown and Wiesel 1961a, b; Arden and Kelsey 1962d). There is less agreement concerning the origin of the increase of the standing potential during light adaptation. Arden and Kelsey (1962d) and Noell (1963) are of the opinion that this increase also originates in the pigment epithelium. According to these authors it would be caused by an interaction between pigment epithelium and rods, due to their increased metabolism after light absorption.

Gouras and Carr (1965), however, drew attention to the absence of increase in the standing potential in cases of occlusion of the central retinal artery, in which condition it is assumed that the deep retinal layers remain intact. In this condition the b-wave of the ERG, whose origin was still located in the bipolar cell layer at that time, is also diminished or extinguished. The authors conclude that the inner nuclear (bipolar) cell layer must be intact in order to generate a normal increase. This does not imply, however, that the increase originates in the bipolar cell layer. Clinically and experimentally there are indications that the standing potential and its increase in light adaptation can be altered independently of the ERG, and that they depend on the intactness of the pigment epithelium (Noell 1963; Krill *et al.* 1966; François *et al.* 1967; Arden 1968; Imaizumi *et al.* 1968; Deutman 1969). Moreover, the b-wave of the ERG is now supposed to originate not in the bipolar cell layer, but in the Müller cells, which extend from the inner side to the outer side of the retina (Dowling 1970). The absence of the increase in the standing potential in occlusion of the central retinal artery may possibly be explained by assuming that the deep retinal layers, although not disturbed anatomically, are disturbed functionally, or that there is a feed-back from the bipolar cell layer or ganglion cell layer to the pigment epithelium.

Since the rod system of the retina far outnumbers the cone system (rods:cones = 20:1), it is not surprising that the standing potential and its light rise may be used primarily as a rod function test. The increase of the standing potential follows the scotopic (= rod) spectral sensitivity curve (Arden and Kelsey 1962d). A small photopic component has been detected by Elenius and Lehtonen (1962).

The standing potential and its increase (LP/DT-ratio) are derived from the bulbus as a whole. Hence a lowered ratio can only be expected in diffuse, and especially deep, retinal disturbances. The classical examples are the tapeto-choroidal and tapeto-retinal degenerations (retinitis pigmentosa). The subnormal LP/DT-ratio found in vitelliform foveal dystrophy (a hereditary condition limited—at least ophthalmoscopically—to the central retinal area) indicates that this condition, notwithstanding its localized nature, must represent a general retinal disturbance (François *et al.* 1967; Deutman 1969).

C. THE ELECTRORETINOGRAM (ERG)

Apart from the determination of the standing potential and its alteration in light adaptation, one is able to record retinal potentials originating from the retina, elicited by light impulses. The recording of these potentials is called electroretinography (ERG). They are usually recorded by means of an electrode placed on

the cornea (the active electrode) against an indifferent electrode on the forehead, eyelid, or at the ear lobe. According to the convention in electroretinography, the recording is made upward when the cornea is positive with respect to the indifferent electrode. This is called a positive response. Known since 1865 (Holmgren), the human ERG came into general use when Riggs (1941) placed the electrode in a contact lens (Fig. 4). Karpe (1945) introduced the ERG into ophthalmological practice.

In reviewing the ERG, three major problems have to be dealt with:

The retinal layers from which the different components of the ERG originate.

The contribution of rod- and cone-mechanisms to the ERG as a whole.

The influence of stray light on the recording.

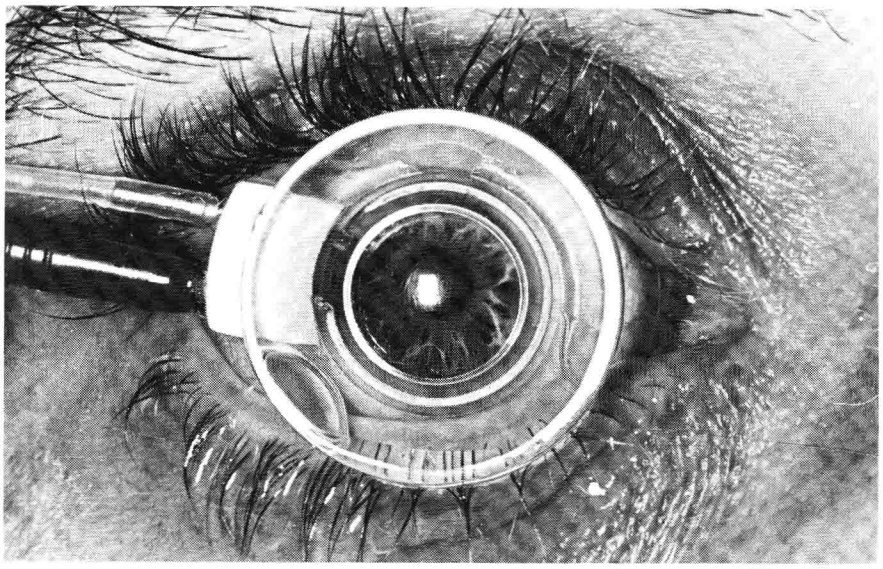

Fig. 4. Henkes' contact lens, with a ring electrode, placed on the eye (see also Sundmark 1962). Note the air bubbles under the contact lens. For good contact between the electrode and the cornea, air bubbles have to be avoided.

1. *Origin of the components of the ERG*

The ERG consists of various components which Einthoven and Jolly (1908) labelled a, b, c and d by analogy with the EKG. The a- and b-waves, as the most important waves, are reproduced in Fig. 5. Later on, the ERP (early receptor potential) and the OPs (oscillatory potentials) were detected. The components of the electroretinogram are slow potentials, originating in cells of the receptor cell layer and bipolar cell layer. Possibly the Müller cells also take part in the response. These cells, extending vertically through the whole retina, are not neuronal cells, but glial cells. The fast spikes of the ganglion cell layer cannot be detected with a contact lens electrode.

Our knowledge in this field has been obtained:

1. With micro-electrodes in animal experiments (Granit 1947, 1955; Svaetichin