HANDBOOK OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

EDITOR-IN-CHIEF A. REMOND

VOLUME 12

Clinical EEG, II

EDITORS: R. HARNER AND R. NAQUET

University of Pennsylvania, Philadelphia, Pa. (U.S.A.) and Laboratoire de Physiologie Nerveuse, Gif-sur-Yvette (France)

Altered States of Consciousness, Coma, Cerebral Death

ELSEVIER

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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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Preface

This volume is intended to be useful for neurologists, neuroanatomists and neurophysiologists who are interested in all aspects of coma and in the related problem of cerebral death.

The first sections deal with the symptomatology of coma, the pathophysiology of altered states of consciousness and the role of electroencephalography in the diagnosis, treatment and prognosis of patients in coma due to anoxia, focal lesions and metabolic disorders. The remaining chapters concern cerebral death which has been studied from several aspects — neurophysiological, clinico-pathological, electrographic and medico-legal.

Even though the authors agree on the electroencephalographic data and on the importance that should be given to them in evaluating cerebral death, some discord remains in the area of terminology. Despite the often judicious reasons advanced by the different co-authors of this volume in defense of the terminology they considered to be most appropriate, the editors have preferred the term "cerebral death", which is in wide use, is not easily misunderstood and is appropriate to the current state of our knowledge concerning the dying process.

Nearly all the articles in this Volume were written between 1971 and 1972. The Editors apologize for the possible absence of references concerning recent years.

Dedication and acknowledgement

This Volume of the Handbook is dedicated to three men who died while actively investigating the criteria for cerebral death:

Daniel Silverman, M.D., November 2, 1971

Robert S. Schwab, M.D., April 6, 1972

Michael G. Saunders, M.D., April 4, 1975

When it was first decided to produce this Volume, Dr. Silverman was asked to be a member of the editorial team. He undertook a large part of the work and his advice and contributions were invaluable.

The section on medico-legal problems was to have been written by Dr. Schwab. His important work was also cut short by sudden death.

The editors were then extremely grateful to Dr. Saunders for taking over the responsibility of the medico-legal section only to be shocked by his unexpected death while the final proofs were being read.

In the sections authored by Silverman and Saunders and in the references to the pioneering work of Schwab, one finds major foundations upon which to build our knowledge of cerebral death. Our thanks and that of future investigators can know no bound.

R. Harner

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Section I. Introduction to Clinical and EEG Studies in Coma

Effective treatment of a comatose patient depends upon an early etiologic and topographic diagnosis and in every case must include measures to avoid neurological, respiratory, circulatory and metabolic complications which are associated with loss of consciousness. This approach to treatment of coma has been emphasized in several monographs (*e.g.*, Tardieu 1942; Fisher 1969; Plum and Posner 1972) and two symposia in Paris have dealt with this topic (*Colloque sur la physiopathologie et le traitement des comas 1962; Les comas—Etudes cliniques et biologiques 1966*).

Faced with the need for immediate therapy of a comatose patient, how may the EEG be helpful and how should it be used? This pertains particularly to increasingly frequent use of EEG in intensive care units, which have habitually requested most studies on patients in coma. In the discussion to follow we shall emphasize the essential clinical elements, review the EEG literature of the past 30 years, present an example of electro-clinical classification of coma, and describe some electrophysiological correlates of the unconscious state.

Our discussion will be directed toward findings in acute loss of consciousness. Abnormalities which may occur during the period of recovery will also be considered, including autonomic disturbances, alterations in behavior, etc., but chronic states of coma will not be included. The duration of the acute phase may depend upon various factors including etiology, severity, age of the patients, etc. These will be discussed together with intercurrent complications.

A. CLINICAL FEATURES

Assessment of cerebral electrical function is generally considered in relation to altered states of consciousness. However, the alteration in consciousness itself in varying degrees of severity is not the only important feature of coma. Tardieu (1942) recalled the importance which Clovis Vincent attached to disturbances of swallowing, especially the early phase during which food or liquid is moved toward the pharyngeal opening. He concluded that this function could only be undertaken when the state of consciousness was virtually normal and he considered mild disturbances of swallowing to be an important sign of impending states of altered awareness.

Plum and Posner (1972) considered five physiological functions which gave particularly valuable information about the level of the brain lesion, the nature of the involvement and the direction that the disease process is taking: (1) the state of consciousness; (2) the pattern of breathing; (3) the size and reactivity of the pupils;

(4) the eye movements and oculo-vestibular responses; and (5) the skeletal muscle motor responses. After considering the mechanisms of functional impairment these authors present a scheme whereby one may decide whether the causal lesion is supratentorial or subtentorial and may evaluate specific etiologies such as tumors, vascular malformations, hemorrhages and infarcts, and various metabolic conditions.

The localizing information provided by alterations in states of consciousness is still controversial. On the other hand, disturbances of those functions the anatomical basis of which is now better understood can be interpreted more accurately. For instance, Plum and Posner go into considerable detail concerning disorders of pupillary action and ocular motility and give a detailed description of the functional anatomy underlying each of these disturbances. Various pupillary abnormalities (apart from those produced by drugs such as scopalomine and atropine) point to the level of the lesion. In the midbrain, damage to the tectal or pretectal region abolishes reactivity to light, the pupils are moderately dilated and fixed, but spontaneous fluctuations in size may persist. Lesions of the midbrain nuclei almost invariably interrupt the sympathetic and parasympathetic ocular pathways resulting in pupils that are irregular, unequal and fixed in midposition. Lesions involving the third nerves in the brain-stem or at their point of emergence produce external oculomotor paralysis and wide dilatation of the pupils. Lesions of the tegmentum of the pons produce pinpoint pupils bilaterally and the light reaction may apparently be abolished for hours. The presence of unilateral Horner's syndrome suggests a lesion in descending lateral brain-stem pathways, most often in the medulla or the cervical cord.

Observations of spontaneous ocular movements and various oculo-cephalic and oculo-vestibular reflexes can provide considerable localizing information in a comatose patient and can be used to differentiate hemispheric lesions, either unilateral or bilateral, from damage to vestibular or oculomotor pathways by direct involvement or compression. If there is marked ocular deviation in the horizontal plane which can still be modified by passive movements of the head or by caloric stimulation, the lesion is almost certainly hemispheric (most often ipsilateral to the direction of gaze). If the ocular deviation cannot be modified, the lesion is very probably in the pons. Fixation of gaze in the neutral position has no localizing value.

These specific features of examination are mentioned to emphasize the need for detailed description of patients in coma. Fisher (1969) has underlined the need for a broad exploration of all residual evidence of neurological function. "Coma can be accurately defined only in terms of a complete neurological examination". Without a description "of the somatic and vegetative accompaniments of coma, information about the nervous system that is comatose remains concealed and the term coma is an abstraction".

Altered respiration is among the most sensitive indicators of central neurological function. Cheyne–Stokes respiration, one of the commonest disorders, is carefully described by Fisher who considered, in contrast to some authors, that it need not carry a grave prognosis. Further, when a patient is deteriorating, Cheyne–Stokes respiration may change into a more regular rhythm at 20–30 breaths per minute with an increase in depth of respiration, accentuation of the inspiratory period, or both.

The neurological events which accompany Cheyne–Stokes respiration (Fischgold and Mathis 1959) often show a cyclical pattern corresponding to that of the respiratory disturbance. During apnea the level of consciousness declines, the patient becomes less reactive, and the eyes may close and deviate upward. Blinking may slow down and stop, pupils contract, the pulse becomes slower, spontaneous movements disappear, and a diffuse hypotonia supervenes. Focal seizures, if present, may diminish or even cease temporarily. At the end of the apneic period when respiration is beginning again, these various functions recover in parallel, suggesting that they form part "of a state of diffuse motor activity of which respiratory activity is one of the principal manifestations". During Cheyne–Stokes respiration, hypercapnea is followed by respiratory arrest. It is obvious that these various cortical-vegetative correlations are extremely complex.

Particular stress should be placed on the study of spontaneous movements and on the reactions produced by various stimuli, verbal, painful and others. Fisher gives special attention to the responses to painful stimulation including bilateral tonic extensor response ("decerebrate" posture, bilateral midbrain or pontine lesions), unilateral tonic response, flexor responses, and combined extensor and flexor responses ("decorticate" posture, bilateral hemispheric disease). In addition to providing information about localization, these signs may also provide information about the severity of the underlying process and the prognosis for recovery.

A more precise account of clinical features is not appropriate to this general survey. The points which have been raised should suffice to indicate that the clinician's responsibility in assessing the severity of states of coma is not only to analyze the degree of unconsciousness, which can vary widely and is difficult to define, but also to evaluate the problem on a larger scale, to examine the major neurological functions and to quantitate the degree of their disturbance as well. It is important to determine the site of the lesion or lesions as well as the most likely etiology if any accurate prognosis is to be given. A similar approach must be taken by the electroencephalographer if his contribution is to be useful. Failure to do so may justify the skepticism expressed by Fisher when he stated that the "electroencephalogram is rarely of crucial help clinically".

B. ELECTROENCEPHALOGRAPHY

1. Background

There have been many publications concerning the EEG in states of coma, as well as a number of symposia, including those in Bombay (Symposium on Coma 1965) and San Francisco (Role of EEG in the Diagnosis of Coma 1970).

The essential facts were published between 1939 and 1963. Among the most important work, the studies conducted by Fischgold *et al.* since 1945 will be referred to most frequently. Their originality lay particularly with the importance which was given to reactivity of the EEG (Fischgold *et al.* 1946, 1955; Fischgold 1957). These studies, summarized in 1959 (Fischgold *et al.* 1959) are still extremely valuable, even

though they were concerned primarily with neurosurgical causes of coma in adults. Almost every aspect of the problem was investigated, including waveforms, reactivity and periodicity. A distinction between disturbance of vigilance and disturbance of consciousness was made, based primarily on clinical data. These studies integrate clinical and electrical phenomena and detail the relations between EEG findings and disturbances in autonomic function, particularly cardiac, respiratory and pupillary changes.

These fundamental investigations were extended in 1963 when Chatrian (Chatrian *et al.* 1963) recognized the appearance of different stages of sleep in patients with coma, which are reviewed in Section V (*e.g.*, Naquet *et al.* 1967; Luecking 1970).

Various studies on toxicology published since 1964 by F. Mellerio and other authors (*e.g.*, Kubicki 1967b; Kurtz *et al.* 1967) have suggested certain parallels with states of anesthesia and have provided a new context in which to demonstrate the EEG changes which accompany states of unconsciousness.

Most reports have been based on visual analysis of the EEG. Automatic analysis has been applied in the study of coma only to a limited extent, despite preliminary work by Fischgold *et al.*, using a Drohocki analyzer (see, more recently, Bergamini *et al.* 1966; Ferillo *et al.* 1969). Since 1966, several more specialized studies have been carried out, for example in the area of evoked potentials (Corletto *et al.* 1966; Arfel 1967; Arfel *et al.* 1967; Bergamini and Bergamasco 1967; Lille *et al.* 1968).

In practice, the gravity of a comatose state is determined by the nature of the etiological process, the location of the central nervous system lesion or lesions, and the depth of unconsciousness (unresponsiveness). To provide useful information about etiology and topography, the EEG must be evaluated in relation to other neurological findings and to the clinical state of the patient as a whole. These aspects are elaborated in the following four sections. It will become apparent that EEG does not often provide diagnostic information which is specific or unequivocal.

It is in the evaluation of depth of coma that the EEG provides most useful information and prognostic perspective. This was clearly demonstrated in the 145 patients reported by Fischgold and Mathis (1959, see Table IV, p. 69) and is confirmed by our study of more than 1,600 comatose subjects since 1958. Such EEG evaluation must be based on two essentials: (1) EEG waveforms; and (2) dynamic studies.

2. *EEG waveforms*

It is no longer necessary to debate whether or not slow waves constitute the main sign of coma. We know that the EEG features of coma are extremely variable, as was noted in early papers such as that of Davis and Davis (1939). Subsequently, Fischgold and Bounes (1946) described the appearance of frontal slow waves on the one hand, but also the intermittent appearance of 10 c/sec rhythms. Mathis *et al.* (1957) concluded that EEG frequency by itself gives no reliable indication of the depth of coma.

Nevertheless, certain abnormalities are encountered more often than others in deep coma. Marked slowing, extreme depression, or intermittent periods of electrical