HANDBOOK OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

EDITOR-IN-CHIEF A. REMOND

VOLUME 2

Electrical Activity from the Neuron to the EEG and EMG

EDITOR: O. CREUTZFELDT

Max-Planck-Institute for Biophysical Chemistry, Göttingen-Nikolausberg (West Germany)

PART C

The Neuronal Generation of the EEG

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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 C

THE NEURONAL GENERATION OF THE EEG

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Introduction

This Part contains 5 sections in which the mechanisms of different EEG-phenomena are discussed on the basis of experimental data. The first Section deals with the cortical electrogenesis of spontaneous EEG-waves, evoked potentials, convulsoid potentials and DC-phenomena. It is shown that different mechanisms may be responsible for different EEG-phenomena, and the possible contribution to EEG-potentials of excitatory post-synaptic potentials (EPSPs) and inhibitory post-synaptic potentials (IPSPs) originating at different parts of the cortical neurones, of abnormal soma depolarizations during convulsions, of axon potentials and of slow extraneuronal potentials are discussed in the context of the volume conductor theory.

The mechanisms of convulsoid and ionic potentials are further elaborated in Section II. In this Section, abnormal neuronal depolarizations in pathological states (paroxysmal activity) and their effect on extraneuronal elements (glia cells) and the extracellular distribution of K^+-ions are demonstrated. The importance of neuronal *vs.* glial and extracellular K^+-distribution for the mechanism of pathological DC-potentials is emphasized.

Section III describes the effects of altered O_2- and CO_2-tensions on neuronal activity (membrane potentials, post-synaptic responses). These data are of significance for neurology as the effect of these different functional states on membrane potentials, EPSPs and IPSPs may explain a number of phenomena during hyperventilation and seizure activity. The correlation of these neuronal effects to simultaneous EEG-phenomena, especially DC-potentials are discussed in Vol. 10A.

Sections IV and V discuss the subcortical mechanisms which are responsible for rhythmical and desynchronized spontaneous EEG-waves. The authors give a re-appraisal of the hypothesis of thalamic origin of rhythmical spindle waves. Based mainly on their own experimental work they demonstrate that the classical hypothesis that rhythmical impulses of midline thalamic origin trigger the cortical waves has to be revised and that phasing mechanisms in the specific projection nuclei have also to be considered.

Section V discusses the desynchronizing effects of the mesencephalic reticular formation in the light of more recent findings on single neurone activity. It is demonstrated that the arousal phenomenon represents a specific organization of neuronal activity rather than just an unorganized, "unspecific" activation of cortical activity.

All articles are mainly based on animal experiments. They represent the present state of our knowledge of basic mechanisms in the generation of EEG-potentials. Each Section is an article in itself and some repetitions could therefore not be avoided. Also some observations may have been interpreted slightly differently by the different authors. The editor did not attempt to smooth out such differences, but rather left

them as they were, since this will give a more realistic picture of the "state of the art" and the still unsolved problems in this field.

The clinical neurophysiologist may ask to what extent these data can be related to the human EEG. It is explicitly or silently assumed by the authors of this Part that the potential phenomena recorded in animals are in principle identical to human EEG-phenomena and that the basic mechanisms for the corresponding potentials are the same. But in the strict scientific sense, the results from animal experiments are only an analogy to human EEG-phenomena. This is especially the case for the comparison between human epileptic EEG-potentials and the pharmacological animal models of paroxysmal activity, but also for other types of EEG-waves, such as the α-rhythm. It was pointed out in several places (*e.g.*, Section I), that there exist differences of EEG-waves and of their mechanisms of generation in different species. Only very few data are yet available from primates, so that the gap between the animal models and the human EEG is still large, if the phylogenetic differentiation of cortical architecture is considered. Especially, it should be left to the discretion of the reader, whether rhythmical spindle waves found in animals, specifically in anaesthetized cats, are analogous to the human α-rhythm. Arguments in favour of such an analogy will be discussed in the respective articles (Sections I and IV), but a definite answer cannot yet be given.

O. CREUTZFELDT
GÖTTINGEN

Section I. Neuronal Basis of EEG-Waves

INTRODUCTION

The existence of small fluctuations in electrical potential at the surface of the cerebral cortex was first reported by Caton in 1875 and independently by Beck in 1890. Caton described spontaneous waves and waves in response to sensory stimulation in rabbits. These potentials were affected by anoxia and anaesthesia, and abolished by death, suggesting that they reflected biological events. Caton recognized the usefulness of these evoked waves for recording localized cerebral events. Práwdicz-Neminski (1925) repeated these experiments and Berger's studies of spontaneous potentials recorded from the scalp of humans gave a first comprehensive description of the human EEG (Berger 1929). However, the electrophysiological mechanism of the EEG remained obscure for more than 30 years.

Since experimental work on the mechanism of EEG-potentials began (Adrian and Yamagiva 1935), various known electrophysiological processes have been considered as generators of EEG-waves. Earlier authors favoured the idea that the EEG represents summated action potentials of cortical neurones (Adrian and Yamagiva 1935; Bishop 1936). However, the fact that EEG-waves could also be observed in states when no action potentials were present during deep anaesthesia (Mountcastle 1957) or hypoxia (Creutzfeldt *et al.* 1957) demonstrated that action potentials could not be the only source of slow surface potentials. The existence of "dendritic potentials" (*i.e.*, slowly propagating potentials in the superficial layers of the cerebral cortex after local stimulation (Adrian 1936; Chang 1951)), suggested a relationship between EEG-waves and activity in the apical dendrites of cortical neurones (Chang 1951; Caspers 1959). However, the existence of activity in deeper layers of the cortex during certain EEG-waves emphasized that deeper structures were also important (Bishop and Clare 1952; Euler and Ricci 1958; Spencer and Brookhart 1961a, b; Calvet *et al.* 1964, etc.). The idea of an oscillating dipole as the source of EEG-potentials (Jung 1963) was derived from findings which showed close relationships between induced or spontaneous cortical DC-potentials and evoked or spontaneous brain waves (Goldring and O'Leary 1951a; Caspers 1959; Landau *et al.* 1964; Fromm and Bond 1967). However, neither the mechanism of the DC-potentials nor their oscillation are explained by such a model. The mechanisms mentioned above may contribute directly to EEG-waves or may influence EEG-activity, but none of them explains EEG-phenomena fully.

The state of our knowledge until 1960 is represented in reviews by Bremer (1958) and Purpura (1959). Indirect evidence led these authors to the hypothesis that at least some EEG-waves were associated with excitatory post-synaptic potentials of cortical nerve cells. By analogy to findings in the spinal cord, Eccles had already proposed a

similar hypothesis in 1951 (Eccles 1951). The close relationship between post-synaptic potentials and the surface EEG was later demonstrated directly by intra- and extracellular recordings from individual cortical cells (Phillips 1961; Creutzfeldt 1964a; Jasper and Stefanis 1965). Even to-day, many questions remain unanswered, but we now have much evidence to support the hypothesis that the main sources of EEG-waves are events on the membranes of the cortical neurones (Creutzfeldt *et al.* 1966b, c). In this Section we give an outline of this evidence, followed by a discussion of some of the problems which have troubled neurophysiologists since the early 1930's and which are still not understood in detail.

Recent reviews on the theme of this Section are given by Jung (1967), Andersen and Andersson (1968), Kullanda (1968), Adey (1969), MacKay (1969), Elul (1972) and Regan (1972). Special aspects are represented in the following reviews: the pacemaker mechanisms of rhythmical EEG-phenomena (Andersen and Andersson 1968); DC-phenomena in relation to EEG-waves (Bishop 1936; Jung 1963; O'Leary and Goldring 1964; Adey 1969); the question of "dendritic potentials" (Chang 1959; O'Leary and Goldring 1964; Purpura 1967; Kullanda 1968); sensory evoked potentials (Chang 1959; Creutzfeldt and Kuhnt 1967, 1972; MacKay 1969; Regan 1972); the statistical nature of cortical EEG-generators (Elul 1972); epileptic phenomena (Creutzfeldt 1969; Scherrer and Calvet 1972). The fact that different conclusions about the generation of EEG-waves are arrived at in different reviews emphasizes the fact that, in spite of our present knowledge in this field, the interpretation of many EEG-phenomena is still difficult.

Significance of animal experiments

Most of the material in this Section is based on results from animal experiments. The application of such results to human EEG-phenomena should be considered carefully.

EEG-waves, *i.e.*, smooth continuous potential changes (corresponding to frequencies up to 50/sec) can be recorded from brain structures of all vertebrates. However, in all invertebrates examined, including annelids, arthropods and molluscs, the dominant character of the electrical activity recorded by surface electrodes is "spiky", looking like single or synchronized nerve impulses (Bullock 1965). There are considerable differences in the frequency components of EEG-waves in different vertebrates, but they have not been systematically investigated. In this Section, we concentrate mainly on the cortical EEG of mammals, and most data are taken from cat, rat or rabbit experiments.

The cat's EEG shows phenomena which are similar to those of the human EEG but there are some differences. The rhythmical waves of the α-range are slower in cats (7–10/sec) than in humans (8–12/sec). They are best expressed in the central areas in cats (Adrian 1941; Lehtinen 1972), whereas in humans they are found mainly in the occipital areas. During relatively deep barbiturate anaesthesia, spindle waves of 5–8/sec are recorded from the whole neocortex of cats. θ-waves (4–6/sec) are more widespread in awake cats than in humans. The θ- and δ-waves seen in sleeping cats are similar to those found in sleeping humans. Since most experiments on cats are

done with direct cortical (ECoG) or bone-implanted electrodes, the attenuating and smoothing effect of the tissue between the electrodes and the electrically active brain is less than in the usual EEG-recordings from the human scalp.

The smoothing effect of the extracerebral tissue has been compared with a low pass filter (De Lucchi *et al.* 1962; Cooper *et al.* 1965; Rayport *et al.* 1966). But it could be simply due to more asynchrony and narrowly focussed localization of fast waves compared with slow waves; in this case, since the layers of the tissue act as an averager over large cortical areas, the scalp recorded EEG-waves would look smoother than the ECoG records.

Cortical origin of EEG-waves

Although it is clear that the pacemakers of most rhythmical EEG-waves are located in subcortical structures, the potentials recorded from the cortex and the scalp are essentially generated within the cortex itself. A cortex slab, which is completely isolated from its afferent inputs, is still capable of responding to direct stimulation with a surface evoked potential (direct cortical response) or, after stronger stimulation, with a "self-sustained after-discharge" also recordable at the surface (Burns 1950; Creutzfeldt and Struck 1962b; Sharpless 1969).[1]

An early description of the strong correlation of rhythmical single unit activity in the pyramidal tract with rhythmical EEG-waves suggested that cortical neurones are involved in EEG-activity (Adrian and Moruzzi 1939). Further experiments corroborated the fact that extracellularly recorded action potentials of cortical cells often show a statistically significant relationship to EEG-waves (Li *et al.* 1953, 1956b; Whitlock *et al.* 1953; Creutzfeldt *et al.* 1957; Creutzfeldt 1963; Jung 1963; Ajmone Marsan 1965). These relationships vary according to the type of EEG-wave. Fig. 1 is a schematic drawing of the relationships found between some types of unitary activity and surface potentials. Some wave types such as spindle waves or paroxysmal potentials show a close relationship with unitary activity, whereas for other types the relationship is looser (Fig. 2). A close relationship between extracellularly recorded action potentials (spontaneous or evoked) and the slow local potentials is often seen, if both are recorded from the same microelectrode (Spencer and Brookhart 1961b; Verzeano 1963; Verzeano *et al.* 1970; Fox and O'Brien 1965; John and Morgades 1969; John 1972).

[1] The view that the EEG-waves recorded from the scalp, especially the α-waves, are not of cortical neuronal origin, has been challenged several times. Concerning human α-waves, a most recent proposal was made by Lippold (1973). He concluded from the close relationship between oscillatory eye movements and the occipital α-waves, that these may be field potentials of ocular muscles rather than of cortical origin. The observations leading to this hypothesis, *i.e.*, the close correlation between eye movements and α-rhythms, are interesting as such, but the hypothesis itself is barely sufficient to account for the actual functional and pathological properties of the human α-waves which can in view of its behaviour in normal and brain diseased patients, only be explained as being of cortical origin.

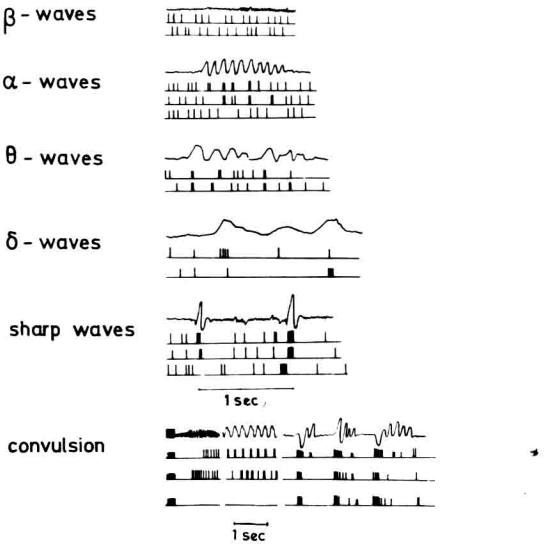

Fig. 1. Schematic presentation of the patterns of single cortical cell discharges during different EEG-waves (after Creutzfeldt 1963). During β-activity, the cortical unit activity is irregular and discharges of pairs of units are not usually correlated. During spindle wave (α) activity, occasional synchrony of unitary discharges can be seen. The mean discharge rate of cortical units decreases during θ- and δ-activity and grouped, synchronized discharges are seen. Local or general application of convulsants, or hypoglycaemia result in sharp EEG-waves together with loosely synchronized high-frequency bursts in many cortical units. During the different stages of a seizure elicited by excessive epicortical stimulation, an initial depolarization block is followed by increased asynchronous discharge (tonic phase) and later by rhythmical synchronized firing of the cortical neurones (clonic phase).

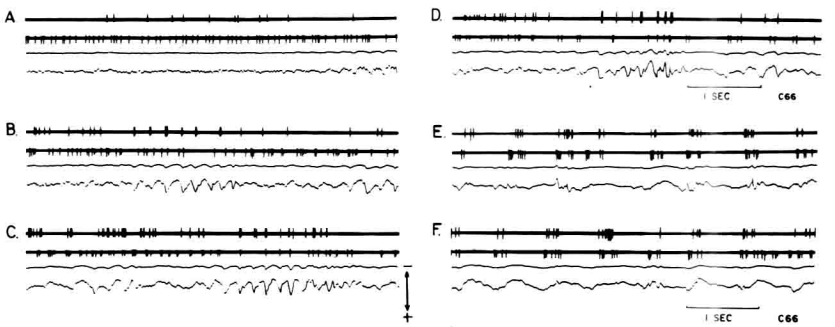

Fig. 2. The discharge activity of two simultaneously recorded cortical units during decreasing levels of blood glucose (from Creutzfeldt 1963). Cat, *encéphale isolé*, recordings from somato-sensory cortex. The two units are separated by about 1.5 mm, monopolar EEG-recording (negativity upwards). $A+B$: Blood sugar level 60 mg %. Arousal type waves in A and spindling EEG with slow θ-waves in B. $C+D$: Blood sugar 45 mg %, E and F: below 30 mg %. Note the increasing tendency towards synchronized grouped discharges separated by silent periods with decreasing blood sugar level.

A. CORTICAL POST-SYNAPTIC POTENTIALS (PSPs)

Since in this Section post-synaptic potentials of cortical neurones will be considered as the main generators of EEG-waves, a description of cortical PSPs is given (for further details see Creutzfeldt *et al.* 1966a, 1969a). One of the main features of PSPs of cortical cells is that they are longer lasting than those of the motoneurones of the

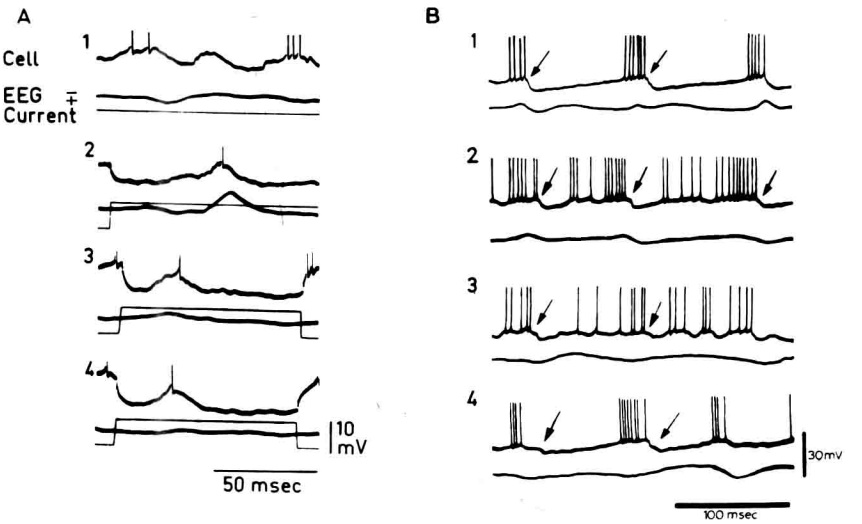

Fig. 3. Spontaneous post-synaptic activity of cortical neurones (from Creutzfeldt 1969a). Cat, nembutal anaesthesia. *A*: All these intracellular records are from the same cell with action potentials chopped. Upper record: Intracellular record. Middle record: Monopolar EEG-record, negativity up. Lower record: Monitoring of intracellular stimulation current. In *A*, 2–4 a polarizing pulse was given in order to prevent some of the EPSPs from reaching firing level. Note that the large post-synaptic depolarizations are composed of grouped EPSPs. The forms of the individual EPSPs look similar in each group, but the 4 different records show different types of EPSPs: steep ones in 1, and increasingly flatter ones in 2–4. The different steepness suggests that the respective synapses are located in different regions of the neurone relative to the recording site (probably the soma). *B*: A different neurone showing spontaneous IPSPs (arrows); they may also appear in groups.

spinal cord (Curtis and Eccles 1959; Creutzfeldt *et al.* 1966a). Excitatory post-synaptic potentials (EPSPs) may have a rise time of several msec and a decay time of 10–30 msec (Li and Chou 1962; Nacimiento *et al.* 1964; Watanabe *et al.* 1966a; Creutzfeldt *et al.* 1969a), while inhibitory post-synaptic potentials (IPSPs) have an even longer duration of 70–150 msec (Albe-Fessard and Buser 1953; Phillips 1959; Klee and Lux 1962; Lux and Klee 1962; Nacimiento *et al.* 1964). Spontaneous EPSPs may appear in isolation or in groups (Phillips 1961). Such groups summate and produce large depolarizing waves (Fig. 3), which in the case of "spindling" reappear at intervals of about 150 msec. In the isolated cortex, spontaneous PSPs have not been observed (Watanabe and Creutzfeldt 1966a). In the intact cortex, IPSPs are less frequent during spontaneous activity than EPSPs and they are of smaller amplitude and shorter duration than those following electrical stimulation of afferent pathways (Watanabe and Creutzfeldt 1966a; Creutzfeldt *et al.* 1969a).

The spontaneous PSP activity is such that the membrane potential of cortical neurones fluctuates most of the time between 3–10 mV below threshold. As a consequence, the spontaneous discharge rate of cortical neurones is low, even in awake animals; it is often below 1/sec and usually below 10/sec (Noda *et al.* 1971). During spontaneous activity, EPSPs of different rise times can be recognized in one cell, suggesting that different synaptic sites are involved (Creutzfeldt *et al.* 1969a) (Fig. 3). The "shape index" method for estimating the site of a synapse in terms of electrotonic

distance from the soma (Rall 1962, see also volume 2B of this Handbook) only allows an estimate of the approximate synaptic distance, since fibres can make multiple synaptic contacts with a cortical neurone. EPSPs evoked by electrical stimulation of the specific thalamic nuclei have a medium-steep slope compatible with a location of synapses on the central trunk of the apical dendrite near the soma, as suggested by anatomical findings (Globus and Scheibel 1966; Szentágothai 1969; Jones and Powell 1970; Garey 1971). On the other hand, EPSPs following transcallosal stimulation have a very slow rise time indicating activity of distant synapses, probably on distal side branches of the apical dendrites according to anatomical observations (Globus and Scheibel 1966). "Recurrent" EPSPs of motor-cortex neurones after antidromic stimulation of pyramidal tract or after (antidromic) stimulation of transcallosal fibres have the steepest slope indicating that the synapses are near the soma (Creutzfeldt *et al.* 1969a). Slow rise time of EPSPs elicited by rhythmical stimulation of non-specific thalamic nuclei (recruiting) and their insensitivity to intracellular stimulation suggest that they may be located distally, perhaps on the apical dendrites (Creutzfeldt and Lux 1964b; Purpura *et al.* 1964a, b). This is in agreement with field potential studies which also indicate that cortical excitation during recruiting waves is located in more superficial layers than excitation during augmenting waves (Li *et al.* 1956a; Spencer and Brookhart 1961a; Sasaki and Prelević 1972) (see below).

1. Developmental aspects

In this context it is interesting to note that during ontogenesis the development of spontaneous EEG-waves and the morphological differentiation of apical dendrites have a comparable time course (Scheibel and Scheibel 1964) (Fig. 4). The EEG of the newborn kitten only contains slow waves of lower amplitude and at this time the apical dendrites have few ramifications and a smooth appearance in Golgi preparations. At this developmental age, only about 1.5% of the cortical synapses contain vesicles (Cragg 1972). When the faster waves appear, some dendritic spines can be distinguished (5 days after birth). When the whole range of spontaneous EEG-waves are present, 10–12 weeks after birth, the dendritic spine distribution (Scheibel and Scheibel 1964) and the synapse counts (Cragg 1972) are like that of the adult. It should be noted, however, that cortical internuncial cells (stellate cells, Golgi II-cells) have a similar developmental time course, and that these intracortical elements may also play a role in EEG-maturation.

Post-synaptic potentials of cortical neurones in the newborn kitten are slower than in adult animals (Purpura *et al.* 1960, 1965c; Purpura 1967). This prolongation is especially noticeable in IPSPs, but also applies to EPSPs. It was therefore suggested that the long latency and duration of cortical evoked potentials in young children may be partly due to the slower time course and transmission time of the cortical and subcortical PSPs rather than to incomplete myelinization alone (Weinmann *et al.* 1965).

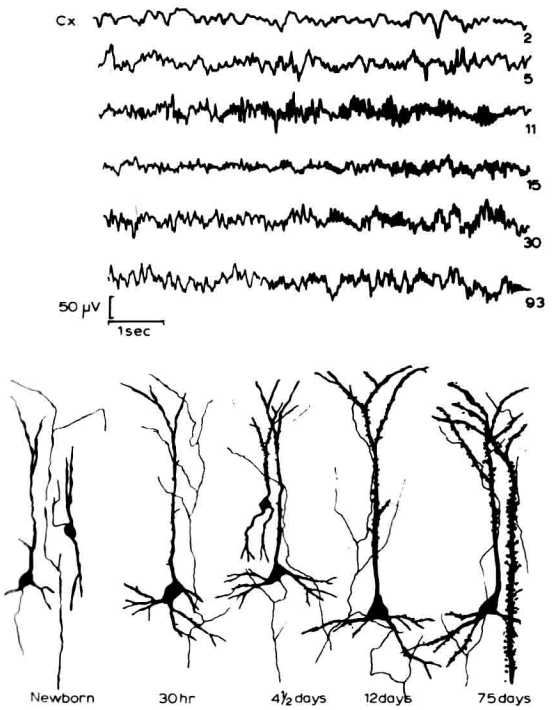

Fig. 4. Structuro-functional relationship between the maturation of the cortical EEG and that of dendrites and synapses of cortical neurones (from Scheibel and Scheibel 1964). Cat. Appearance of first spindle activity by the 11th day and of increasingly mature, "alpha-rich" records by the 30th day. By the 93rd day the adult type is seen. The drawings below summarize the development of dendrites and dendritic spines of cortical pyramids and their synaptic relations with afferent fibres (Golgi-preparation).

B. RELATIONSHIP BETWEEN SPONTANEOUS EEG-WAVES AND THE SYNAPTIC ACTIVITY OF SINGLE CORTICAL NEURONES

Before discussing the generation of cortical EEG-waves, we shall give a mainly phenomenological description of the relationship between cellular activity and different types of EEG-activity. It will be seen that the correlation between surface waves and cellular activity is different for different types of EEG-waves.

1. Rhythmical spindle waves in cats

Spindle waves in the awake cat have a frequency between 7 and 10/sec, but are slower under nembutal anaesthesia. It has been known for some time that cortical neurones tend to discharge in close relationship to the spindle waves (see above). However, the individual waves are more closely related to subthreshold depolarizations of the cortical neurones, *i.e.*, summated post-synaptic potentials (Creutzfeldt *et al.* 1964a, 1966b; Jasper and Stefanis 1965). The relationship is such that the surface negative potentials of the waves coincide with the cellular depolarizations. As seen in Fig. 5, the relation is not absolute, and a certain scatter between individual EEG-waves and the depolarizations of any one cell is always observed. The rhythmical depolarizations of a

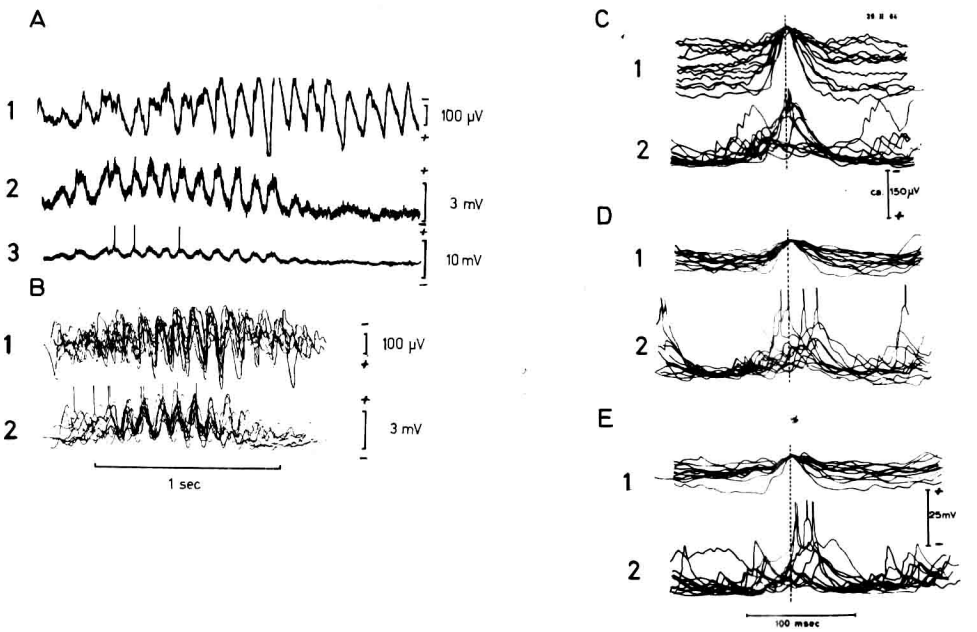

Fig. 5. Spontaneous spindle waves with simultaneously recorded intracellular potentials of a cortical neurone (*A–B*: from Mergenhagen *et al.* 1968; *C–E* from Creutzfeldt *et al.* 1966c). Cat, somato-sensory cortex. *A*: 9–10/sec spindle waves during drowsiness. 1: Monopolar EEG-record (negativity up); 2 and 3: Intracellular recording with high (2) and low (3) amplification, DC-records. *B*: Several spindle periods from the same experiment, graphically superimposed EEG- and intracellular records. Note the close correspondence between the surface negative spindle waves and the post-synaptic depolarizations of the cell. *C–E*: Spindle waves during barbiturate anaesthesia from a different experiment. Individual waves from one "spindle" in each drawing (*C–E*), the EEG on top (monopolar recording, negativity up), the intracellular record below (depolarization up). *C*: Waves from a spindle with high amplitude, *D–E* from spindles with lower amplitudes. Note the close, though not absolute temporal link between the individual waves and the post-synaptic cellular depolarizations.

given cell may start earlier or last longer than the correspondent EEG-spindles (Fig. 5, *B*). This slight variation in the degree of "synchronization" is not surprising, since the activity in the neuronal pools of the thalamic relay nuclei, which generate the cortical EPSPs during spindle activity, is not absolutely synchronous and seems to "circulate" in these thalamic neuronal networks (Verzeano *et al.* 1960b, 1970; Andersen and Andersson 1968, see also Section IV). In some records, the cellular depolarizations during spindle waves are smooth and without discernible steps, but often steps caused by the individual EPSPs of one "burst" can be recognized on the compound depolarizations (Fig. 3, *A*). Even in such a case it is possible that compound post-synaptic depolarizations consisting of several EPSP-steps may be produced by only one afferent fibre which discharges in rhythmical bursts. The model of Fig. 6 for rhythmical spindle waves is based on these findings and on those reported in Section IV as well as later in this Section.

IPSPs of cortical cells do not seem to play a major role during spindling. One rarely sees prominent individual IPSPs between the grouped EPSPs. This may be due to the fact that the rhythmical EPSPs during spindling often do not reach the threshold so

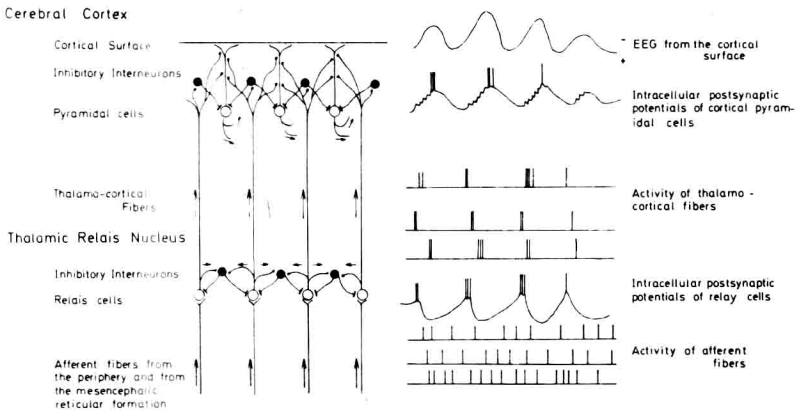

Fig. 6. Schematic model of the electro-physiological basis of spindle waves. It is assumed that the essentially tonic, random input into the specific relay nuclei is transformed into excitatory–inhibitory cycles by the recurrent inhibitory mechanisms in the specific thalamic relay nuclei. This results in synchronous bursts of thalamo-cortical fibre activity. The excitatory post-synaptic potentials of the cortical neurones (especially high on the apical dendrites) are associated with surface negative EEG-waves. The cortical EPSPs may, but need not, reach the firing level. IPSPs from inhibitory cortical circuits activated either directly by thalamo-cortical afferent or indirectly by intra-cortical recurrent fibres are not regularly seen between the post-synaptic depolarizations.

that relatively little spike activity and thus little inhibition through recurrent collaterals is elicited. It is possible that some continuous inhibition may underly the rhythmical excitations during spindling, only being revealed if the cell membrane is depolarized by injury or by anodal current injection through the intracellular electrode (Purpura and Shofer 1964a).

2. *Slower waves (θ- and δ-waves) in cats*

Only few studies have been published on the relationship between neuronal activity and the slow waves which correspond to the human θ- or δ-waves. Some data are available from sleep studies (Creutzfeldt and Jung 1961a), also from hypoglycaemia (Creutzfeldt and Meisch 1963; Mergenhagen *et al.* 1968), anaesthesia and hypoxia (Creutzfeldt *et al.* 1957) studies. If the EEG shows increased δ-activity, the overall discharge rate of cortical unit activity decreases. This is more marked in the case of pathological δ-activity (hypoxia, hypoglycaemia or anaesthesia) than during normal sleep, where some neurones may even increase their discharge rate during the slow wave period (Creutzfeldt and Jung 1961a; Evarts 1962, 1964; Noda and Adey 1970). However the discharge pattern clearly changes during slower wave activity. Grouped discharges are found during θ-activity, especially if there are "sharp" components (see below). If θ-waves appear in "dysrhythmic" groups as for example during hypoglycaemia, the neuronal discharges tend to fall into step with these waves as during spindling (Fig. 2). The discharge probabilities are lower during δ-waves than during waves in the θ- and α-range; often only subthreshold post-synaptic depolarizations are seen. Also, the phase relationship between δ-waves and neuronal events is less consistent than in the case of α- or θ-waves. It is possible that under abnormal