

Neurophysiologic Basis of EEG and DC Potentials

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CHAPTER

2

The clinical electroencephalographer correlates central nervous system (CNS) functions as well as dysfunctions and diseases with certain patterns of the electroencephalogram (EEG) on an empirical basis. Obviously, this method has been found valuable in clinical practice. Therefore, why should the clinical electroencephalographer study the basic elementary processes underlying the EEG? There is little doubt that the range of EEG interpretations can be much widened and misinterpretations avoided when the underlying elementary processes are also considered. This is true especially for convulsive disorders and cerebral metabolic disturbances. For example, an isoelectric EEG can be caused by selective $p\text{CO}_2$ increase while the brain is sufficiently supplied with O_2 . On the other hand, in the presence of practically normal $p\text{CO}_2$ levels, cerebral hypoxia may be the cause. It will be pointed out below that the prognosis may be quite different in these two cases.

POTENTIAL GENERATION AT NEURONAL AND GLIAL ELEMENTS: MEMBRANE POTENTIALS AND FIELD POTENTIALS

The basic mechanisms that give rise to potentials recorded outside the CNS elements will be described. Such extracellular potentials are generally known as field potentials (1).

In the course of this presentation, the morphology of generator structures is discussed briefly. Then, the electrical activity demonstrable with intracellular recordings from neurons and glia cells is described. On the basis of this information, the principles of the generation of extracellular field potentials are outlined and the various types of field potentials are characterized.

GENERATOR STRUCTURES

The CNS essentially consists of nerve cells and glia cells. The arrangement of neurons usually shows a specific type of laminar character. Glia cells are located between neurons. As shown in Figure 2.1, several processes emerge from the nucleus-containing cellular soma (body) of the nerve cell. These processes can be divided into two types according to their function. Most of the processes are dendrites that branch off into numerous small ramifications. Every cell also has an axon that may split up into multiple collaterals. Such an axon provides contact with other nerve cells or with other target organs. In the case of interneuronal connections, the contact consists of synapses that cover the dendrites, the soma, and the axon hillock in large numbers. Thus, nerve cells are usually covered with several

thousand synapses (2). The glia cells are imbedded between nerve cell somata, dendrites, and axons. They usually have several processes that make contact with somata and processes of nerve cells; they may also make contact with vessels. This histologic arrangement results in a cerebral extracellular space consisting of very narrow intercellular clefts (De Robertis and Carrea, 1965).

NEURONAL MEMBRANE POTENTIALS: INTRACELLULAR RECORDINGS

Essential potentials that can be demonstrated with intracellular recordings are characterized briefly. When the membrane of the nerve cell body is penetrated by a microelectrode, a potential of about 60 to 70 mV with negative polarity in the intracellular space can be recorded. This membrane potential is subject to various fluctuations that are elicited chiefly by synaptic activities. Their mechanisms are shown in greater detail in Figure 2.2. As can be derived from this schematic illustration, the neuron

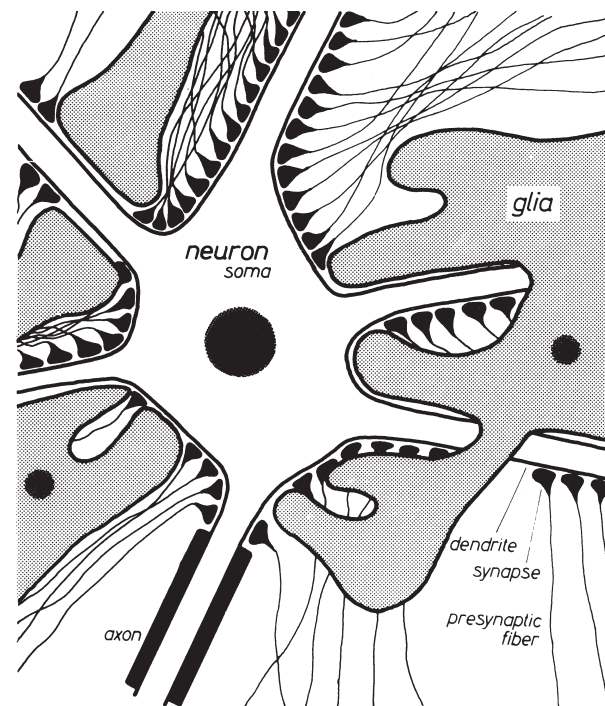


Figure 2.1 Schematic drawing of morphology and histology of neuronal and glial elements.

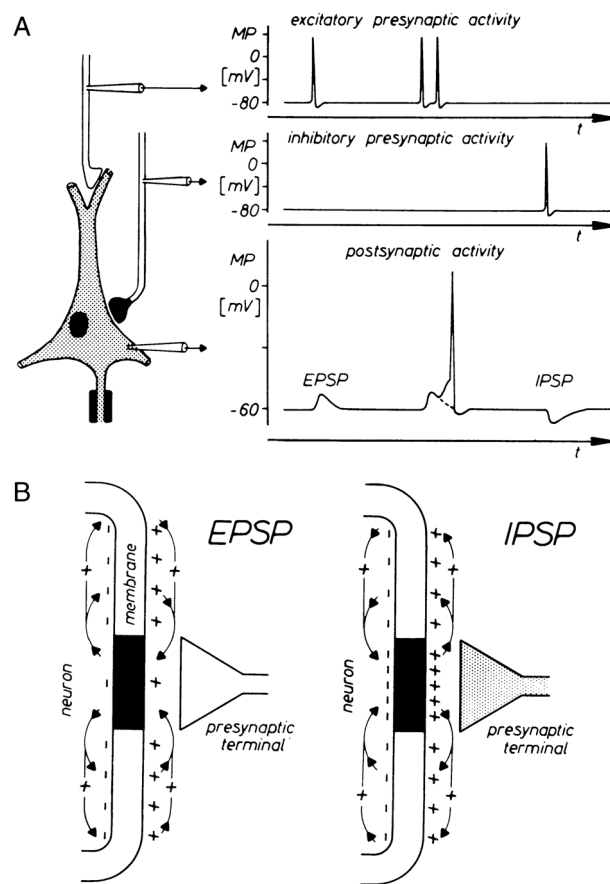


Figure 2.2 Membrane potential (MP) changes and current flows during synaptic activation. **A:** The MP of the postsynaptic neuron and the MP of the presynaptic fibers are recorded by means of intracellular microelectrodes. Action potentials in the excitatory and inhibitory presynaptic fiber lead to excitatory postsynaptic potential (EPSP) and inhibitory postsynaptic potential (IPSP), respectively, in the postsynaptic neuron. Two EPSPs sum up to a superthreshold potential, triggering an action potential in the postsynaptic neuron. **B:** During EPSP and IPSP, ionic current flows occur through as well as along the neuronal membrane, as shown by arrows. The density of + and - signs indicate the polarization of the subsynaptic (dark area) as well as that of the postsynaptic membrane during synaptic activation.

from which the soma membrane potential is recorded has synaptic connections. The corresponding presynaptic structures are also explored with microelectrodes. If an action potential travels along the fiber, which ends in an excitatory synapse, an excitatory postsynaptic potential (EPSP) occurs in the following neuron (Fig. 2.2A). If two action potentials travel along the same fiber with a short interval, there will be a summation of EPSP triggering an action potential on the postsynaptic neuron after reaching the membrane threshold. If an action potential travels along a fiber ending in an inhibitory synapse, then hyperpolarization will occur, representing an inhibitory postsynaptic potential (IPSP) (3–5).

Because of the time course of the various membrane potential fluctuations, the postsynaptic potentials are thought to

contribute primarily to the generation of the extracellular field potentials in question (1,4,6,7). For this reason, the ionic mechanisms of these potentials are discussed in greater detail. The individual events of this process are presented with a magnified time base (Fig. 2.3). With the elicitation of an EPSP, a net inflow of cations occurs across the subsynaptic membrane. As shown in Figure 2.2B, a potential gradient develops along the neuronal membrane in the intra- and extracellular spaces. Because of this potential gradient, cations move along the nerve cell membrane through the extracellular space in the direction of the subsynaptic region. An inversely directed flow takes place in the intracellular space. With the generation of an IPSP, there is an outflow of cations from the nerve cell and/or an inflow of anions into the nerve cell. These changes first increase the membrane potential at the subsynaptic membrane in comparison with the surrounding segments of the membrane. For this reason, a potential gradient develops along the nerve cell membrane, as in the case of the EPSP genesis. This potential gradient causes, in the extracellular space, a flow of cations from the subsynaptic region to the surrounding portions of the membrane. An inverse process develops in the intracellular space (4).

The ion fluxes in the extracellular space are of paramount significance in the generation of field potentials. Therefore, these processes are further discussed in the following chapters.

GLIAL MEMBRANE POTENTIALS: INTRACELLULAR RECORDINGS

In addition to the neurons, glial cells may also play a role in the generation of extracellular field potentials (8,9). Therefore, the bioelectric properties of glial cells are summarized.

If a glial cell is penetrated with a microelectrode, a membrane potential can be recorded with a polarity similar to that of the nerve cells. The size of this membrane potential approximates the potassium equilibrium potential and hence somewhat exceeds the membrane potential of nerve cells. In contrast to neurons, glial cells fail to show any action potentials, and there are also no postsynaptic potentials. Thus, in contrast to neurons, glial cells do not show characteristic potentials that distinguish them unmistakably from other cells. The glial membrane potential, however, is also not constant. An augmentation of the extracellular potassium concentration (potassium activity) causes depolarization of glial cells (Fig. 2.4A). Concentration changes of other ions cause only negligible alterations of the glial cell membrane potential. The glial cell is hence comparable to a potassium electrode (8,10).

The dependency of the glial membrane potential on the extracellular potassium concentration is the reason for a functional linkage with adjacent neuronal structures. Neuronal activity is associated with outflow of potassium ions. As shown schematically in Figure 2.4B, repetitive firing of neurons gives rise to increased extracellular potassium concentration and hence to glial cell depolarization (11,12). If the potassium concentration does not affect the entire glial cell membrane and remains increased only locally, then potential gradients build up along the glial cell, giving rise to

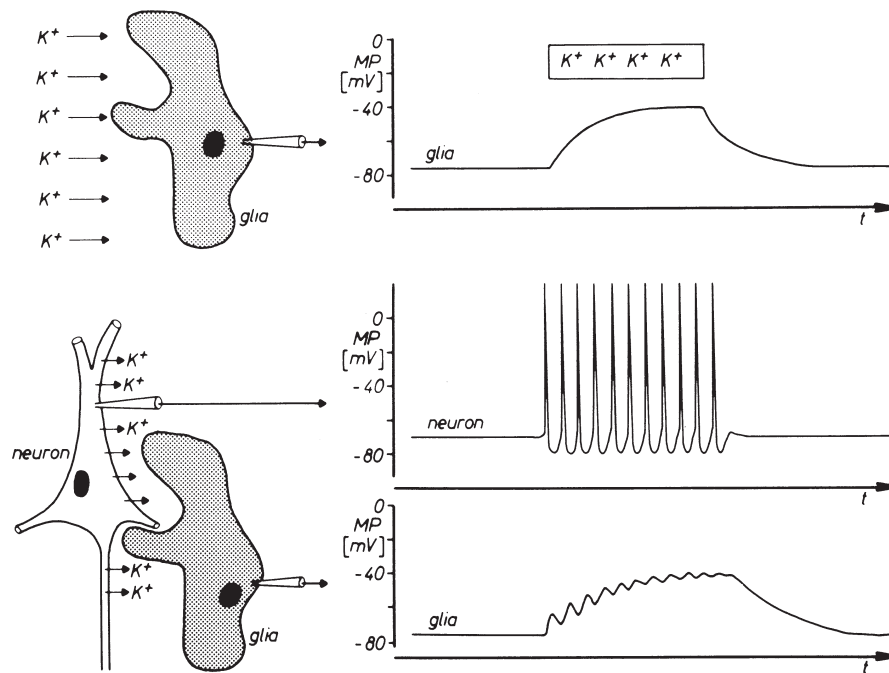


Figure 2.3 Basic mechanisms underlying generation of potentials (electroencephalogram [EEG]) and of magnetic fields (magnetoencephalogram [MEG]) in the extracellular space of central nervous system. The description is based on the assumption that an extended neuronal process, for example, a dendrite, is locally depolarized by activation of an excitatory synapse.

intra- and extracellular current flows similar to the ones described in reference to neuronal synaptic transmissions (Fig. 2.2). Glial cells frequently have widespread processes and furthermore may have close connections with each other. For this reason, potential fields of considerable spatial

extension may develop on the basis of the aforementioned mechanisms (1,9,13,14). In view of the above-described functional interconnections, it is quite likely that in the genesis of extracellular field potentials an amplifying effect can be attributed to the glial cells.

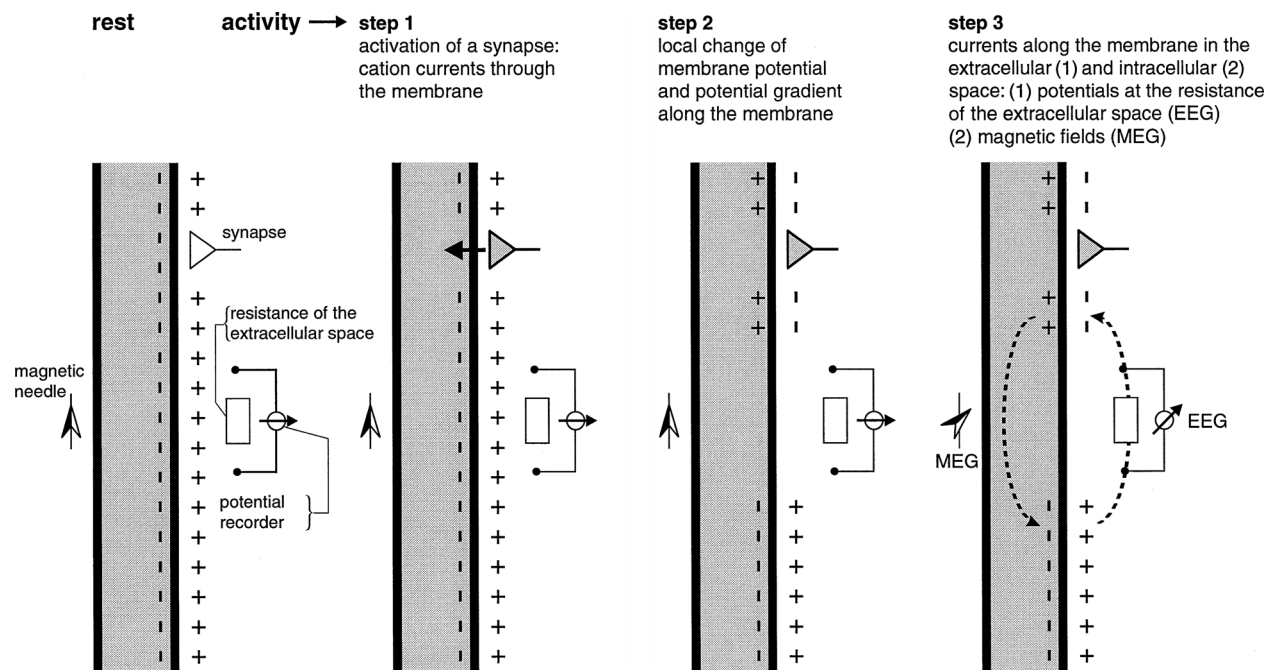


Figure 2.4 Membrane potential (MP) changes of glia cells induced by an increase in the extracellular K^+ concentration (arrows in the schematic drawings). **A:** Potassium is applied extracellularly to the glia cell. **B:** The potassium concentration is increased due to an activation of a neighboring neuron. (From original tracings from Kuffler SW, Nicholls JG, Orkand RK. Physiological properties of glial cells in the central nervous system of amphibia. *J Neurophysiol.* 1966;29:768–787.)

FIELD POTENTIALS

It has been shown in the preceding section that primary transmembranous currents generate secondary ionic currents along the cell membranes in the intra- and extracellular spaces. The portion of these currents that flows through the extracellular space is directly responsible for the generation of field potentials (Fig. 2.3). Particular significance must be ascribed to the synaptic processes as causing events for the field potentials in question, especially for their time course. In accordance with these statements, the generation of extracellular field potentials will be discussed as exemplified by extracellular fields accompanying synaptic activity (4,7,14,15). The discussion of these events will again make use of a very protracted time axis (Fig. 2.3). The explanation of the events is given in reference to the schematic view in Figure 2.5. This figure shows a widely stretched neuronal element, with one end segment lying close to the surface of a central nervous structure. At both ends of this neuronal unit, the microelectrodes ME_1 and ME_2 are inserted. At the same time, the extracellular electrodes E_1 and E_2 are located at the surface and at the deeper end of the neuronal element. The potentials picked up from the intra- and extracellular electrodes are shown in the vicinity of each electrode. The potential recorded from the surface of the nervous structure is accentuated by *thicker lines*. Figure 2.5 shows active excitatory and inhibitory synapses, either close to the surface or located in the depth. As described elsewhere, the activation of an excitatory synapse leads to a net inward flow of cations. If this statement is applied to Figure 2.5A1, then it becomes evident that the upper end of the neuronal element will be depolarized in comparison with other segments of the same cell. Accordingly, the synaptic current flow causes an EPSP at the microelectrode ME_1 . This local depolarization then gives rise to further intra- and extracellular ionic currents along the nerve cell membrane. Because of the intracellular movements of positive charges, depolarization in the area of microelectrode ME_2 also takes place. This depolarization, however, is less steep and of smaller amplitude. At the superficially located extracellular electrode E_2 , the inflow of positive charges into the neuronal element causes a negative field potential. The extracellular electrode E_1 is, metaphorically speaking, approached by positive charges so that a positive field potential will develop in this area. The point of reversal of the field potentials is localized between electrodes E_1 and E_2 . The exact position of the point of reversal depends on the distribution of extracellular impedances.

Current flows of reversed direction (in reference to the recording electrodes) will occur if the active excitatory synapse is located at the deeper end of the neuronal element (Fig. 2.5A2). In this case, positive charges approach the superficially located electrode (E_1) (again speaking metaphorically) and remove themselves from the deeply located electrode (E_2). This arrangement of the active synaptic structures causes a positive field potential at the surface and a negative one at the deep electrode. The current flows accompanying the activation of inhibitory synapses located in deeper and in more superficial areas, respectively, are shown in Figure 2.5B. As can be derived from this illustration, the activation of a deep inhibitory

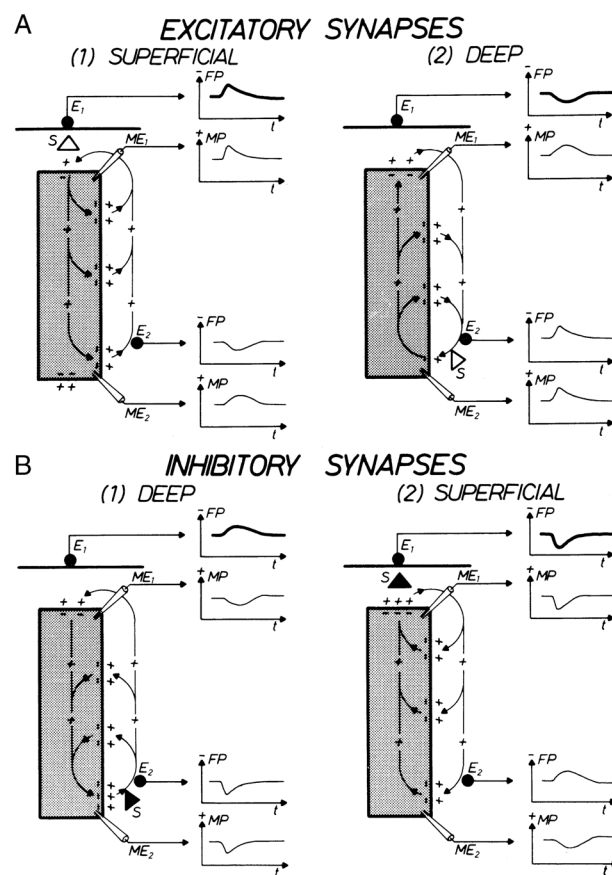


Figure 2.5 Membrane potential (MP) changes and field potentials (FPs) elicited by the activation of excitatory and inhibitory synapses in the central nervous system. The elementary processes are explained by means of a neuronal element (*hatched area*), the one end of which contracts the surface of a structure in the central nervous system. The MP of the neuron element is recorded at both ends by the microelectrodes ME_1 and ME_2 . The extracellular field is picked up at the surface of the neuronal structure by the electrode E_1 , as well as in the vicinity of ME_2 by the electrode E_2 . Active excitatory and inhibitory synapses are marked by *open triangles* and *black triangles* (S), respectively. **A1:** The inward current at S generates an EPSP that appears in the region of ME_1 , as well as in that of ME_2 . Because S is located superficially, the FP generated, due to the direction of the extracellular current flow (*arrows*), is of negative polarity at the surface (E_1) and of positive polarity in the deeper recording (E_2). **A2:** The activation of a deep excitatory synapse elicits a current flow with inverse direction as compared with **A1**. Therefore, the extracellular FP consists of a positive deflection at the surface and a negative one at the depth. **B1:** The outward current at S generates an IPSP in the region of ME_2 , as well as in that of ME_1 . Due to the direction of the extracellular current flow, the FP generated consists of a positive fluctuation in the depth (E_2) and a negative one in the surface recording (E_1). **B2:** The current flow during the activation of a superficial inhibitory synapse is inverse as compared with **B1**. Therefore, the FP recorded from the surface consists of a positive fluctuation. Differences in the time course of the various potentials are caused by the electrical properties of the tissue.

synapse (Fig. 2.5B1) produces a current flow that is largely similar to the one generated by the activation of a superficial excitatory synapse (Fig. 2.5A1). In the same manner, there are also similar current flows in the extracellular space when a superficial inhibitory synapse (Fig. 2.5B2) or a deeply located excitatory synapse (Fig. 2.5A2) is activated. Accordingly, a negative field potential will develop at the surface of a central nervous structure (in the schematic view of Fig. 2.5) whenever a superficial excitatory or a more deeply located inhibitory synapse is activated. The corresponding principle applies to generation of the superficial field potentials of positive polarity.

Due to their higher densities especially the currents flowing through the intracellular spaces give rise to magnetic fields surrounding the elements. These magnetic fields can be picked up from the scalp as magnetoencephalogram (MEG; Fig. 2.3).

Types of Field Potentials

The field potentials, whose generation has been described, can be subdivided into different types. If field potentials are recorded against an inactive reference point with an upper frequency limit of about 100 Hz, then two types of field potentials can be distinguished, depending on the time constant of the amplifying recording device. In the case of a time constant of 1 second or less, the extracellular field potentials correspond with that which is commonly known as the EEG. If the recording is carried out with an infinite time constant, that is, with direct current (DC) amplifier, then slower potentials can also be picked up. Potentials recorded with this technique are generally known as DC potentials (1,7,14,16). Thus, DC potentials comprise slow as well as fast field potentials. The fast components correspond with the potential fluctuations of the EEG. Due to different time constants, however, the faster potential components may differ from each other as far as their time course is concerned when recordings are done either with conventional EEG amplifiers or with DC amplifiers.

Thus far, technical problems have made it difficult to carry out DC recordings from the scalp. Except for special areas of application, DC recordings are usually performed in animal experiments. DC potentials directly reflect the state of activity of central nervous cells and therefore contribute to the explanation of the mechanisms of genesis of cerebral field potentials (13,17). For this reason, DC potentials will be discussed jointly with EEG waves.

For the sake of comparison, Figure 2.6 shows the EEG and the DC potentials during convulsive activity, hypercapnia, and asphyxia. As shown in this illustration, a tonic-clonic convulsion is associated with a negative DC shift (7,12–14,18–20). Furthermore, it can be seen that the hypercapnia-induced disappearance of the EEG is associated with a monophasic positive DC shift. In the case of EEG extinction due to primary asphyxia, however, there are characteristic patterns of DC fluctuation. Hence, similar findings in the conventional EEG may be associated with different DC shifts.

Original Remarks Made By Ernst Niedermeyer

What does the term *DC shift* mean? What is DC? Speaking from experience, many electroencephalographers have no clear

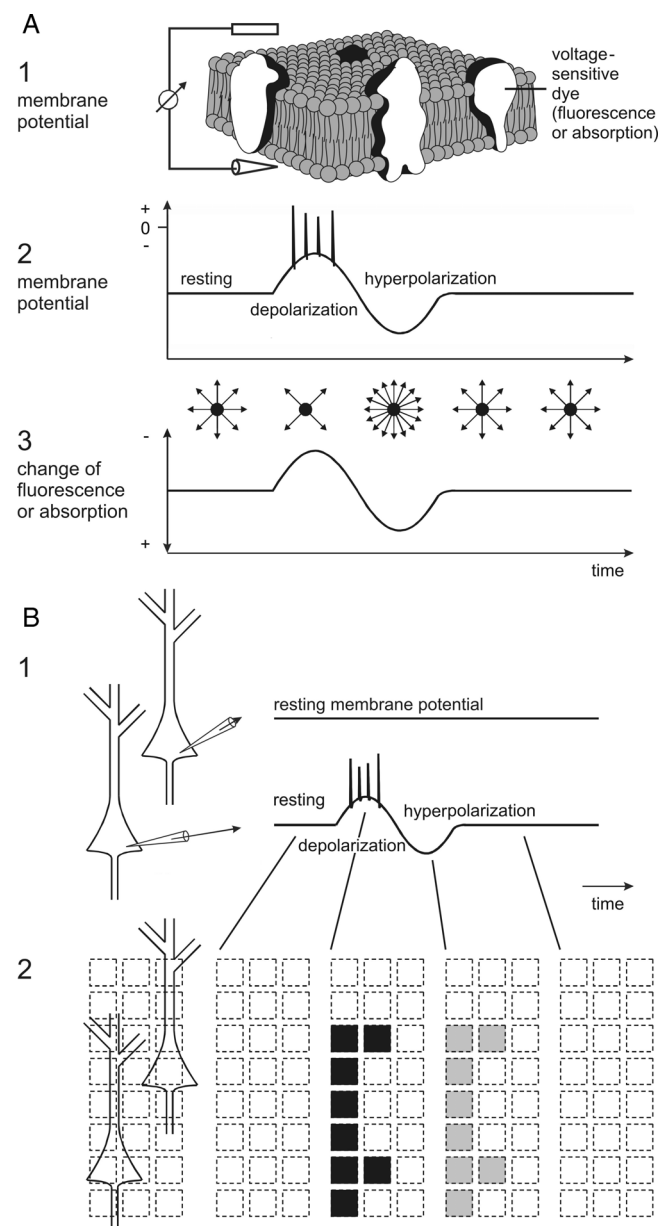


Figure 2.6 Recording of neuronal membrane potentials using voltage-sensitive dyes, and principles and schematic example of application. **A:** (1) A dye is incorporated into the double lipid membrane of nerve cells and illuminated by light with dye-specific wave length; simultaneously the membrane potential is recorded with an intracellular micro-electrode against a reference electrode in the extracellular space. (2) Changes of the membrane potential (MP) starting from the resting level passing a decrease (depolarization) with action potentials superimposed and a subsequent increase (hyperpolarization) and eventually returning to resting level. (3) In correspondence to the different MP levels fluorescence and absorption of the dye change. With fluorescent dyes a depolarization is associated with a decrease and a hyperpolarization with an increase of fluorescence (symbols). **B:** (1) Two neurons in a population; one stays in the resting state and the other changes its MP as in A2. (2) By the aid of a microscope and a connected array of diodes (squares) the different MP changes of both neurons can be detected via the different optical behaviors. (Speckmann E-J. *Das Gehirn meiner Kunst. Kreativität und das selbstbewußteGehirn*. Münster: Daedalus; 2008.)

6 Part I ■ Basic Principles

concept regarding DC potentials or DC shifts. One cannot blame them because, for strange reasons, “DC” has two meanings in this context:

1. DC means direct current (and this is, of course, commonplace): a current without oscillations; a current derived from a battery source; a current maintained in one direction through a circuit. A more imperfect DC is produced by a rectifier, used to change alternating current (AC) into DC. For multilingual readers, DC is *courant continu* in French, *Gleichstrom* in German, and *corrente continuo* in Italian.

Electroneurophysiologically, DC shifts are ultraslow potentials, about as slow as 0.1 to 0.2/sec. This, however, is not true DC. Such slow activity is just a bit more “DC-like” since it does not show the faster “AC-like” activity. One simply has to live with this kind of misnomer.

2. DC also means direct coupling (and this is much less known). What coupling? The coupling between the stages of EEG amplification. Conventional EEG machines have stages coupled by capacitors. Now one has to remember that capacitors (a) reject DC and (b) determine the time constant. Even a very long time constant (several seconds duration) may not suffice for the recording of DC potentials. Direct coupling is a capacitor-free coupling between the stages of amplification and provides the optimal condition for DC recording. This is technically quite difficult in clinical conventional EEG recording but easier under experimental neurophysiological conditions in animals.

Hence, be aware of the dual significance of the term *DC* (also see the section Filters).

Validation of Field Potentials As To Their Functional Significance

Correlating field potentials with other signals accompanying neuronal activity may contribute to a validation of them. There is a variety of methods other than electroencephalography for detecting brain activity. Thus, single photon emission tomography (SPECT), positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and intrinsic optical imaging (IOI) are based on metabolic changes associated with increases of local neuronal activity. The latter methods are “very indirect” (21). Electroencephalography (EEG) including evoked potentials (EP) and magnetoencephalography (MEG) represent “more direct ones” since they measure the field effects of the proper neuronal activity and therewith of the information processing brain activity. For the analysis of neuronal network functions, the immediate and simultaneous recording of membrane potentials of all neurons in a population by application of voltage-sensitive dyes is the “only direct” method available yet (22–27). All these methods have advantages and disadvantages. Thus, the functional imaging using voltage-sensitive dyes cannot be applied in patients for several reasons, for example, prerequisite of direct access to the brain structure to be investigated, phototoxicity, and pharmacologic side effects of the dyes. But, this method is helpful to analyze the principles of functional meaning of field potentials in living human brain slices in vitro, especially with spontaneously occurring epileptic discharges.

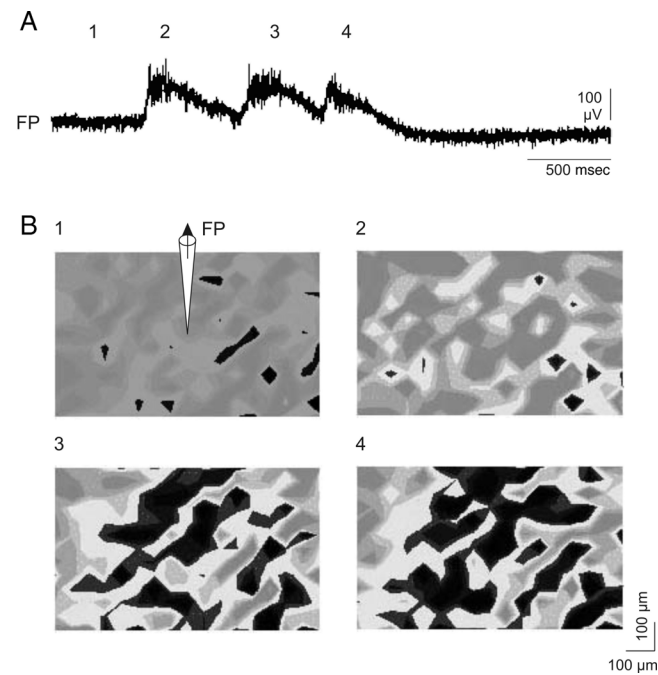


Figure 2.7 Simultaneous detection of membrane potentials (MP) of all neurons in a population (voltage-sensitive dye) and conventional recording of the local field potential (FP) at the same time. Living brain tissue (0.5 mm thick) from the temporal lobe of a patient who underwent epilepsy surgery. **A:** Recording of the local FP (“local EEG”). (1) Resting state; (2 to 4) epileptic discharges of different intensities. Epileptic discharges appeared spontaneously, that is, they were not induced experimentally. **B:** MP changes indicated by the intensity of fluorescence of the dye (black, decrease of the MP, depolarization). Similar epileptic potentials in the FP (2 and 3) are associated with different extents of neuronal depolarizations and similar extents of neuronal depolarizations with different epileptic potentials in the FP (3 and 4). (Speckmann E-J. *Das Gehirn meiner Kunst. Kreativität und das selbstbewußte Gehirn*. Münster: Daedalus; 2008.)

A principle and schematic example of recording neuronal membrane potentials using voltage-sensitive dyes is displayed in Figure 2.7. The living brain slices are stained with fluorescence (or absorption) dyes (Fig. 2.7A1). With depolarization and hyperpolarization the fluorescence is decreased and increased, respectively (Fig. 2.7A2 and A3). The changes in fluorescence are measured via a microscope by an array of detectors and therewith the actual membrane potentials of the neurons are observed (Fig. 2.7B1 and B2).

The method of simultaneous measurement of neuronal membrane potentials of all neurons in a population is successfully applied in living human brain slices (0.5 mm thick) in vitro obtained from neurosurgical interventions (tumor and epilepsy surgery) (24–26,28).

A comparison of the field potentials, that is, the local EEG, and of the neuronal membrane potentials detected by the aid of voltage-sensitive dyes is given in Figure 2.8. The tissue is a slice preparation from the temporal neocortex resected from a patient suffering from pharmacoresistant complex partial

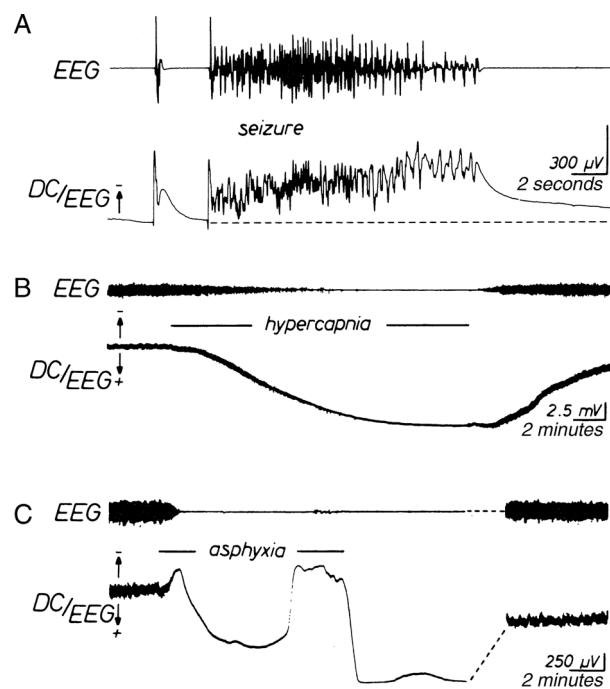


Figure 2.8 EEG (time constant: 1 second; upper frequency limit: 100 Hz) and DC/EEG recordings (DC recording: upper frequency limit, 100 Hz) during a generalized seizure induced by pentylenetetrazol (A), during hypercapnia (B), and during asphyxia (C). Original recordings were obtained from cats and rats. Note the different time scales.

seizures. Most of these living human brain slices show spontaneous epileptic EEG potentials, that is, epileptic discharges not induced by experimental procedures. One can derive the following from the recordings:

1. During epileptic discharges only a certain portion of the neurons in the population is active simultaneously, that is, a complete synchronization is missing (Fig. 2.7, numbers 2 to 4).
2. Similar epileptic potentials in the EEG (Fig. 2.7, numbers 2 and 3) are associated with different extents of neuronal depolarizations and similar extents of neuronal depolarizations with different epileptic potentials in the EEG (numbers 3 and 4).

WAVE GENERATION

In the preceding sections, the generation of single field potentials was described. In this section, the principles of the generation of wavelike potential fluctuations are outlined. This is followed by the discussion of the laminar distribution of such potentials in the cerebral cortex.

To present the generation of wavelike potential fluctuations on the surface of a central nervous structure, a simple model as shown in Figure 2.9 is used. This model consists of two extended pyramidal neurons of vertical orientation. Terminals of afferent fibers make contact with the superficial dendrites of both neurons via excitatory synapses. The bioelectrical activity of these structures is recorded with intracellular microelec-

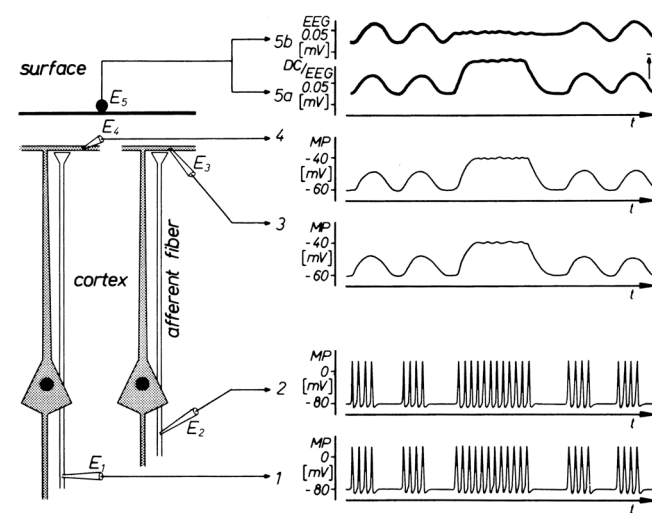


Figure 2.9 Principles of wave generation. The excitatory synapses of two afferent fibers contact the superficial dendritic arborization of two longitudinal neuronal elements. The afferent fiber activity is recorded by means of the intracellular electrodes E₁ and E₂, and the membrane potentials (MPs) of the dendritic elements are recorded by the electrodes E₃ and E₄. The field potential at the surface of the neuronal structure (cortex) is led by the electrode E₅. Synchronized groups of action potentials in the afferent fibers (E₁, E₂) generate wavelike EPSPs in the dendritic areas (E₃, E₄) and corresponding field potentials in the EEG and DC/EEG recording (E₅). Tonic activity in the afferent fibers results in a long-lasting EPSP with small fluctuations. During this period the EEG (5b) shows only a reduction in amplitude, whereas the DC/EEG recording (5a) reflects the depolarization of the neuronal elements as well.

trodes. The microelectrodes E₁ and E₂ are located in the ascending fibers and the microelectrodes E₃ and E₄ are in the superficial dendrites of the postsynaptic neurons. To pick up the extracellular field potentials, the electrode E₅ lies on the surface of the central nervous structure.

As shown in tracings 1 and 2, action potentials occur synchronously in the afferent fibers. There are grouped discharges that are temporarily supplanted by tonic activity. The ascending action potentials elicit individual EPSP in the upper dendrites of the neurons; these EPSPs are subsequently summated into major depolarizations in accordance with the discharge frequency. As shown in tracings 3 and 4, amplitude and duration of the depolarizations depend on the discharge pattern of the afferent fibers. The synaptic activity at the superficial structures gives rise to extracellular current flows resulting in superficial field potentials. With the use of DC recording techniques, the superficial field potentials reflect the potential fluctuations of the dendritic membrane. If, however, the superficial field potentials are recorded with a time constant of 1 second or less, then only the fast fluctuations of the superficial field potentials are demonstrable.

Thus far, the principles of genesis of EEG and DC waves have been shown in the schematic view of Figure 2.9. Accordingly, the generation of physiologic EEG waves may be explained as follows. If a grouped and synchronous influx takes place in afferent fiber systems toward the superficial

generator structures, then EEG waves evolve that are of high amplitude and distinctly separated from each other. In case of a periodic sequence of the afferent bursts, the recording of the field potentials shows sinusoidal potential fluctuations. This mechanism has been presumed by several groups of investigators as the principle of the generation of the alpha rhythm and slower periodic EEG waves. According to these workers, thalamocortical feedback loops are believed to play a significant role in the generation of the alpha rhythm (see Chapters 3 and 4 for detailed descriptions of the generation of rhythmic activities) (1,29).

If the afferent influx of impulses occurs at a high frequency for a longer period and/or synchronously, then negative field potentials with small fluctuations will result from the extracellular current flows. Accordingly, the EEG recording will pick up only waves of smaller amplitude and mostly higher frequency. In the DC recording, however, the prolonged depolarization of the superficial structures caused by the afferent high-frequency influx will express itself by a negative DC potential shift (30,31). There is a close correlation between the amplitude of the negative DC shift and average discharge frequency in the afferent fiber systems. This mechanism may apply principally to the generation of beta activity and other EEG waves of higher frequencies (see also cortical sources of beta and gamma rhythms in Chapter 3 and Fig. 3.16). A decrease of the amplitudes of the EEG waves can also occur when the afferent activity is diminished. In this case, however, the depression of EEG waves is accompanied by a positive DC shift (see Fig. 2.17) (32).

The principles of generation of individual and wavelike field potentials at the surface of central nervous structures such as the cerebral cortex have been described. If the wavelike potential fluctuations are recorded not only from the cortical surface, but also from different cortical layers, then it can be shown that potential fluctuations in the latter recordings may differ considerably from those at the surface. These differences imply polarity, frequency, and amplitude (1,33,34). Such a recording from the cortex of the rat is shown in Figure 2.10. According to this illustration, field potentials reverse their polarity between electrode 1 (on the surface) and electrode 2 (located 300 μ m beneath the cortical surface). Two and sometimes more of such phase reversals may be observed in deeper recording sites depending on the experimental conditions (phase reversals of alpha oscillations are shown in Chapter 3, Figs. 3.9 and 3.10). The vertical distribution type of field potential will be discussed in greater detail in connection with the generation of cortical field potentials during convulsive activity.

In the course of the discussion of cerebral field potentials, it was pointed out that particular significance must be attributed to synaptic activity. A view of the laminar distribution of neurons in the cortex and the dense coverage of these unitary structures with synapses makes it clear that different patterns of potentials must necessarily occur in different layers when populations of synapses are activated in a different manner. This should be clarified by the schematic drawing in Figure 2.10.

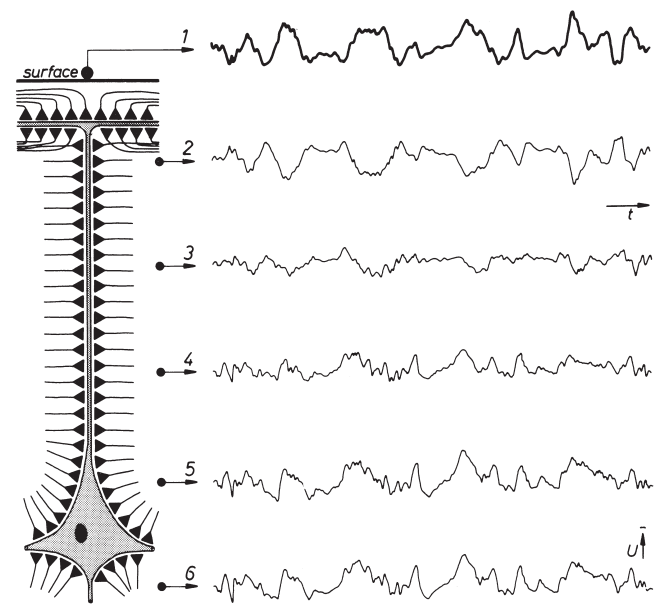


Figure 2.10 Surface (1) and laminar recordings (2 to 6) of EEG waves of the cortex. The schematic drawing symbolizes conical neuronal elements densely packed with synapses. (Drawings from original tracings obtained in experiments in the rat's motor cortex during pentobarbital anesthesia.)

CORTICAL FIELD POTENTIALS DURING EPILEPTIFORM ACTIVITY

In the following subsections, the generation of cortical field potentials during convulsive activity is discussed. The first subsection deals with focal activity, and the second discusses generalized tonic-clonic convulsive activity. For methodical reasons, we refer to data derived from experimental work in animals.

Focal Activity

If a convulsive substance such as penicillin is applied to the surface of the cerebral cortex, steep negative potentials of high amplitude can be picked up from the area of application after a short latency period. These discharges repeat themselves in stereotyped form and periodicity (Fig. 2.11A) (12,35,36). If the membrane potential of a cortical neuron is simultaneously recorded with a microelectrode while a second microelectrode picks up the corresponding field potentials, then potential fluctuations occur as shown in Figure 2.11B. It can be derived from this illustration that the monotonously recurrent negative field potentials are associated with equally stereotyped membrane potential fluctuations. These oscillations of the membrane commence with a steep depolarization that, having exceeded the membrane threshold, triggers a series of action potentials. This is followed by a plateau that, after 80 to 100 msec, changes into a steep repolarization, and frequently also into a hyperpolarization. These membrane potential fluctuations have proved to be characteristic in the epileptiform activity of individual neurons. They are generally known as paroxysmal depolarization shifts (PDSs) (12,37).

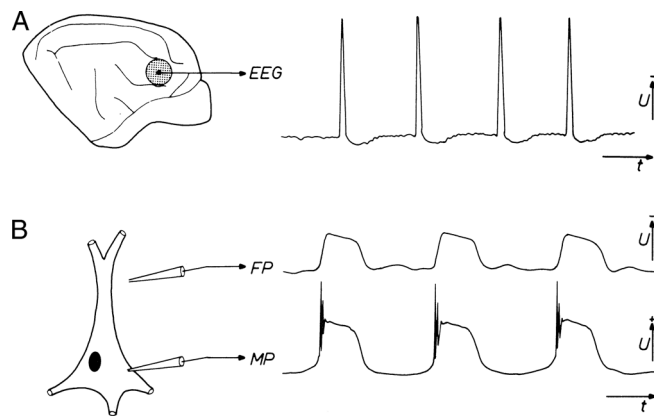


Figure 2.11 EEG (A) and membrane potential (MP)_A changes of a pyramidal tract neuron and extracellular field potential (FP) recorded in the vicinity of the impaled neuron (B) during focal interictal activity elicited by application of penicillin to the cortical surface (*hatched area* in A). Drawings of original tracings from experiments in the rat. The sweep speed in B is five times that in A. The recording sites are shown in the schematic drawings.

Investigation of potential distribution within the cerebral cortex after the local application of penicillin yields a variety of findings. An appropriate model is shown in Figure 2.12. In this experiment, recordings of interictal field potentials were carried out from the cortical surface, from inside the cortex, and from the spinal cord. The spinal field potentials permit the observation of electrical activity descending from the cortex to the spinal cord. In Figure 2.12A, negative field potentials are recorded from the cortical surface and from the two upper intracortical contacts after the application of penicillin together with penicillin-metabolizing enzyme penicillinase.

There are, however, field potentials with predominantly positive components in the deeper contacts 4 to 6. If penicillin is applied to the surface without penicillinase, then negative field potential will also develop in deeper cortical layers. If it is assumed that the negative field potentials mirror the direct epileptiform activity of neuronal structures (Fig. 2.11), then it must also be assumed that deeper cortical elements are involved in convulsive activity shown in of Figure 2.12B in contrast with Figure 2.12A. This is further supported by the observation that neuronal activity descending to the spinal cord and producing characteristic spinal field potentials occurs only under the experimental conditions shown in Figure 2.12B. If one compares the recordings in Figure 2.12A and B, it becomes clear that, with a monotonous epileptiform potential at the cortical surface, the intracortical potential distribution and the occurrence of descending activity may differ considerably (33,38–43).

If penicillin is applied to deeper cortical laminae (Fig. 2.12C), then negative field potentials will be confined to that region. These potentials are consistently accompanied by descending activity to the spinal cord. Under these conditions, there is frequently nothing but a positive potential fluctuation of minor amplitude at the cortical surface (33,39).

In summary, it can be derived from the described experimental models that, in focal convulsive activity limited to the cortex, the surface potential does not necessarily reflect the bioelectrical events in deeper cortical layers.

Generalized Tonic–Clonic Activity

Here, possible mechanisms involved in the generation of cortical field potentials during tonic–clonic convulsive activity are described. Again, data are based on experimental observations in animals. Tonic–clonic convulsive activity was triggered by repeated injections of pentylenetetrazol (also see Refs. 12 and 36).

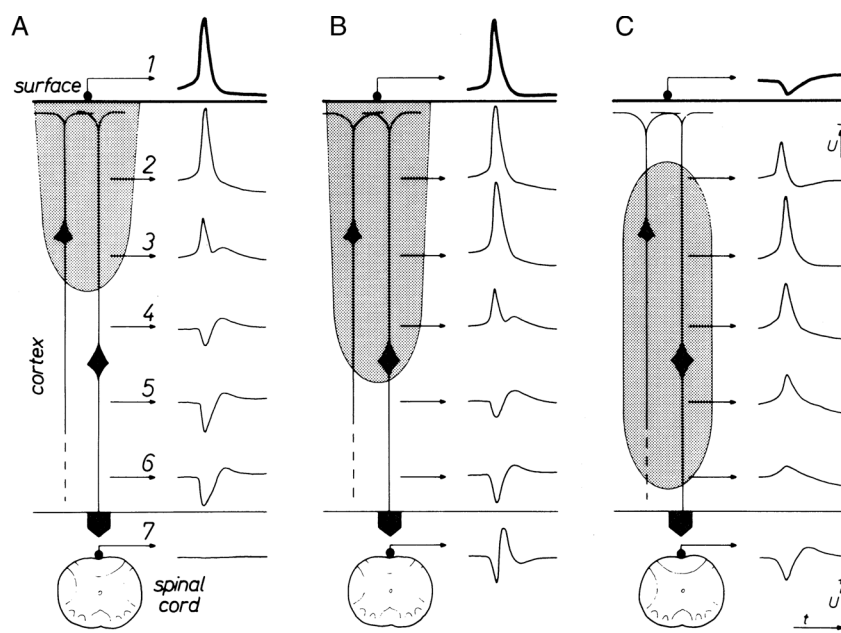


Figure 2.12 Cortical field potentials recorded at the surface (1) and from within the cortex (2 to 6) and spinal field potentials (7) during interictal activity. The interictal activity was elicited by penicillin. **A,B:** Potential distribution after surface application of the drug. In A, the spread of penicillin is limited by the use of penicillinase. **C:** Potential distribution after intra-cortical application of penicillin at recording point 4. The areas directly involved in the epileptiform activity as indicated by negative field potentials are marked by hatching in the schematic drawings. Spinal field potentials are linked to the occurrence of negative field potentials in lamina V (B and C, 4). Distance between the intracortical electrodes, 300 μ m. (From original tracings from Elger CE, Speckmann EJ, Caspers H, et al. Focal interictal epileptiform discharges in the cortex of the rat: laminar restriction and its consequences for activity descending to the spinal cord. In: Klee MR, Lux HD, Speckmann EJ, eds. *Physiology and Pharmacology of Epileptogenic Phenomena*. New York, NY: Raven Press; 1981.)

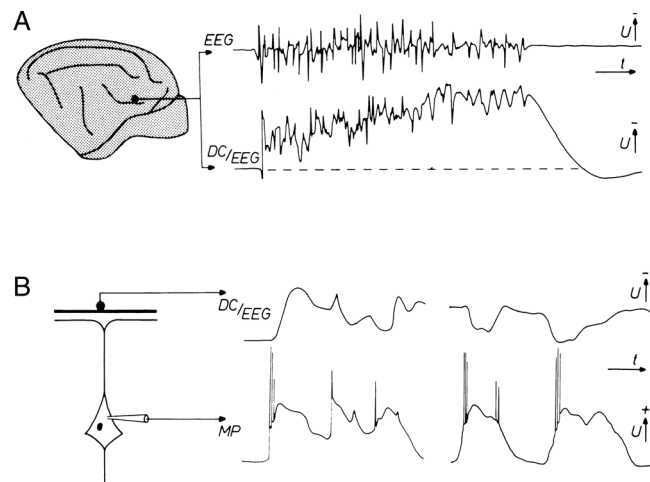


Figure 2.13 Simultaneous recordings of EEG and DC/EEG (**A**) and of DC/EEG and membrane potential (MP) of a pyramidal tract neuron (**B**) during generalized tonic-clonic seizures elicited by pentylenetetrazol. (Drawings after original tracings from experiments in the cat's motor cortex. The sweep speed in **B** is 10 times that in **A**.)

Figure 2.13A shows a tonic-clonic convulsion recorded with a conventional EEG amplifier, as well as with a DC amplifier. There is a negative DC shift from the baseline during a convulsive seizure. This negative DC shift gradually recedes during the termination of the convulsions and frequently changes into a transient positive after shift (12–14,17,18,20,40).

When the membrane potential of a pyramidal tract neuron of lamina V is recorded during a convulsive seizure, it can be shown that under these conditions typical PDSs become manifest (Fig. 2.13B). If these PDSs are correlated with the potential fluctuations in the DC recording, it can be noticed that the PDSs in pyramidal tract neurons are coupled at the beginning of the convulsive seizure with superficial negative potential fluctuations and at the end of the convulsive seizure with surface-positive potential fluctuations (Fig. 2.11B) (1,17,44).

In addition to the field potentials of the cortical surface and the membrane potentials of the pyramidal tract cells, field potentials were also recorded in the fifth lamina. Under these conditions, it can be shown that every PDS is associated with a negative monophasic field potential in the depth (Fig. 2.14A). These stereotyped potential fluctuations in deep cortical layers correspond with field potentials at the cortical surface with either monophasic negative or positive (Fig. 2.14A1 and A3) or with polyphasic (Fig. 2.14A2) configurations. This statement does not merely apply to individual ictal potentials but is also true for prolonged trains of potentials during the convulsion. As Figure 2.14B shows, paroxysmal depolarizations of pyramidal tract cells may be accompanied by a sequence of either negative or positive potentials on the cortical surface. If one correlates these various field potentials on the cortical surface with the slow DC shifts occurring during the convulsion (also see Fig. 2.14A), then it can be demonstrated that the surface-negative field potentials are associated primarily with a slight DC shift and that surface-positive field potentials will appear

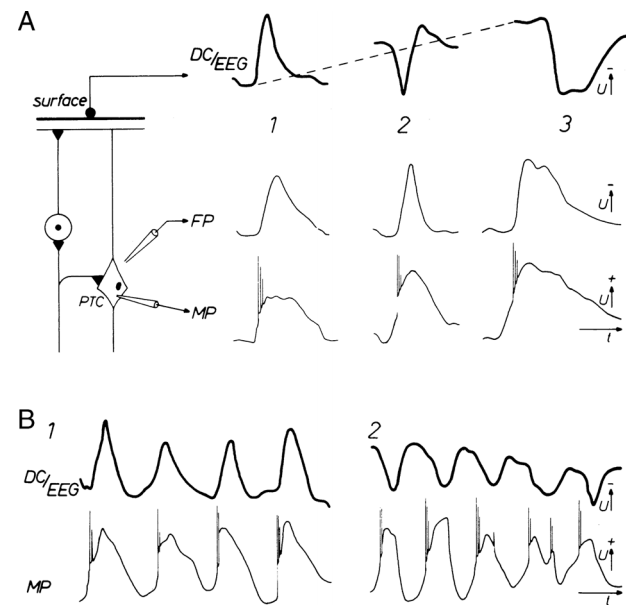


Figure 2.14 Single potential fluctuations at the cortical surface (DC/EEG) and concomitant membrane potential (MP) of a pyramidal tract cell (PTC) and field potentials (FP) in the PTC layer during generalized tonic-clonic seizures. The seizure activity was induced by pentylenetetrazol. **A**: The negative potential (1), the positive-negative fluctuation (2), and the positive potential (3) in the DC/EEG recording coincide with monophasic negative FP and stereotyped paroxysmal depolarization shift in the neuron. The negative DC shift occurring during the seizure is indicated by a dashed line in the upper row. Monophasic negative potentials in the DC/EEG recording occur with small and monophasic positive fluctuations along with a marked DC displacement. **B**: The relations between DC/EEG potentials and MP of PTC as described for **A1** and **A3** also hold true for trains of potentials (1 and 2). (From original tracings from Speckmann EJ, Caspers H, Jansen RWC. Laminar distribution of cortical field potentials in relation to neuronal field activities during seizure discharges. In: Brazier MAB, Petsche H. eds. *Architectonics of the Cerebral Cortex, IBRO Monograph Series*. Vol 3. New York, NY: Raven Press; 1978:191–209.)

when the negative DC shift at the cortical surface reaches and exceeds a critical value (1,17,44,45).

These data are interpreted with flow charts in Figure 2.15. The amplitude of the negative DC shift at the cortical surface depends greatly on the amount of the afferent influx of impulses to the generator structures in the superficial cortical laminae. This predominantly asynchronous afferent influx is symbolized by the width of hatched arrows in Figure 2.15. Accordingly, the afferent influx in Figure 2.15A is smaller than that in Figure 2.15B. Therefore, there is a smaller DC shift in Figure 2.15A and a prominent one in Figure 2.15B. In the case of Figure 2.15A, a synchronized inflow of impulses from sub-cortical structures is assumed to reach the cortex (widened afferent fiber in schematic view). As a consequence, pyramidal tract cells will be stimulated to generate a PDS, and structures close to the surface will be depolarized through the mediation of interneurons. Accordingly, in such a constellation of

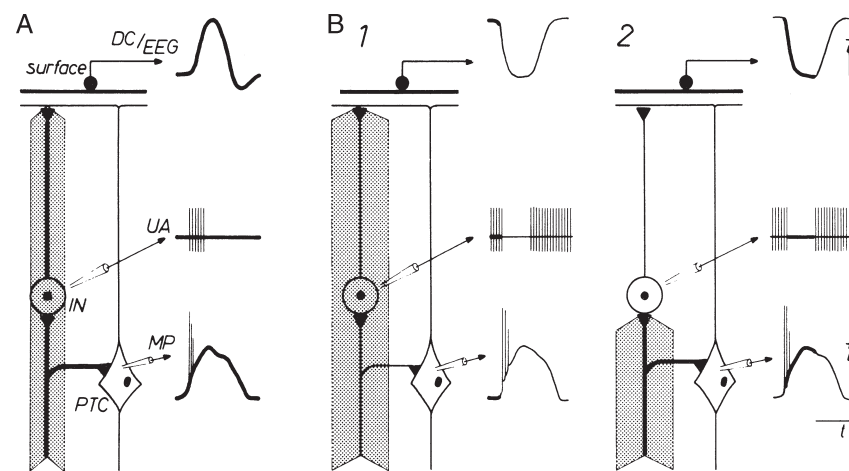


Figure 2.15 Flow charts of neuronal processes possibly responsible for the generation of DC/EEG waves of opposite polarity during a generalized tonic-clonic seizure. (*Hatched arrows*) Symbols for continuous asynchronous input to the cortex; (*heavy lines*) symbols for phasic volleys giving rise to single convulsive discharges; (*PTC*) pyramidal tract cell; (*IN*) interneuron; (*MP*) membrane potential; (*UA*) extracellularly recorded unit activity. **A:** During a moderate asynchronous input to the cortex (*small hatched arrow*), a burst of UA triggers a paroxysmal depolarization shift in a PTC. Simultaneously, it leads to a depolarization of superficial neuronal structures and therewith to a negative fluctuation in the DC/EEG recording at the cortical surface. **B:** With an increased asynchronous input to the cortex (*wide hatched arrow*), the DC potential shifts to a more negative level than in **A** (1). When in these conditions a phasic volley reaches the cortex, paroxysmal depolarization shifts are also triggered in PTC, whereas the enhanced asynchronous UA is interrupted mainly due to inactivation. The latter process results in a disfacilitation of the upper neuronal structures and therewith to a positive fluctuation of the superficial DC/EEG potential (2). (From original tracings from Speckmann EJ, Caspers H, Jansen RWC. Laminar distribution of cortical fluid potentials in relation to neuronal field activities during seizure discharges. In: Brazier MAB, Petsche H, eds. *Architectonics of the Cerebral Cortex. IBRO Monograph Series*. Vol 3. New York, NY: Raven Press; 1978:191–209.)

excitatory processes, the paroxysmal depolarization in the depth will be coupled with a surface-negative field potential. With augmentation of the already existing afferent inflow of impulses, the interneurons involved will necessarily exhibit a heightened level of excitation (Fig. 2.15B). If an additional highly synchronized afferent influx of impulses takes place under these conditions, then further PDSs will be triggered in the pyramidal tract cells, but, in the interneurons, the previously existing high-frequency activity will be temporarily interrupted, chiefly due to inactivation. This causes a decline of the excitatory inflow of impulses to the superficial cortical structures. This disfacilitation gives rise to a positive field potential at the cortical surface. In this manner, a massive afferent inflow of impulses provides the basis for a correlation of positive epicortical field potentials with stereotyped paroxysmal depolarizations and monophasic negative field potentials in the depth (17,44).

SPREADING DEPRESSION

In this section, the generation and propagation of cortical field potentials during spreading depression (SD) is discussed. SD is a strong and rapid depolarization of neuronal tissues and propagates slowly (3 to 5 mm/min) as a wave in brain tissue (46). The SD phenomenon is exclusive to the CNS and appears to influence both the neuronal and the glial cells. The most

characteristic physiologic feature of SD is a negative DC potential shift with maximal amplitude of 5 to 30 mV and duration of 30 to 90 seconds (Fig. 2.16A) (47). SD recordings by extracellular microelectrodes inserted into the gray matter of the neocortex demonstrate that SD can be biphasic or triphasic with the main negative component. SD begins with a first small positive component that is sometimes not observed. The main feature of the SD is a negative wave of high amplitude, which is then followed by a positive-going wave of smaller amplitude, but longer duration. The white matter beneath the neocortical gray substance becomes positive, while the gray matter itself undergoes the negative wave. Apical dendrites were preferentially involved in the generation of the negative DC deflection. When recordings were made in hippocampal CA1 region, SD invariably started earlier and ended later in the layer of the dendritic trees than among the cell body. SD flows in the opposite direction compared with the current underlying tonic-clonic seizure discharges, which is inward in the neuron soma layers (47,48).

A brief period of excitation heralds SD, which is immediately followed by prolonged neuronal activity depression. This is replaced by a sustained increase in the neuronal activity; SD also produces transient suppression of synaptic transmission that is replaced by a sustained increase in the efficacy of synaptic transmission. SD significantly enhanced the amplitude of fEPSP following a transient suppressive period and increased

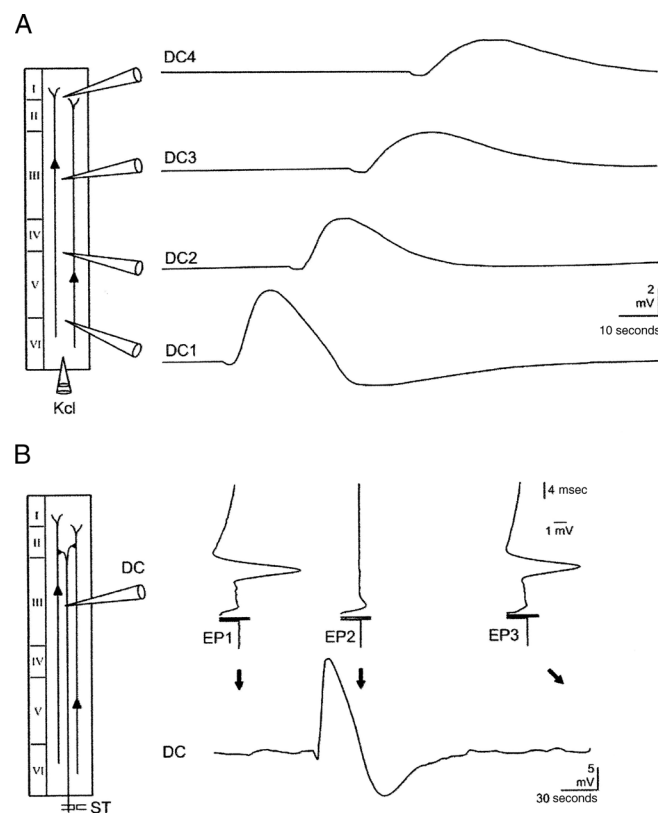


Figure 2.16 Propagation of negative DC potential shift in the neocortex and its effect on neuronal excitability. **A:** Recording of slow spread of negative DC potential wave after injection of KCl in human neocortical tissue. Voltage variations were recorded simultaneously by four electrodes (DC1 to DC4), which are set apart by 1 mm. KCl was injected in layer VI. Injecting and recording electrodes arranged as shown. **B:** Suppression of evoked potentials (EP) during spreading of negative DC potential fluctuation. The DC potential was recorded from layer III of a human neocortical slice. EP was elicited by a single electrical stimulation (ST) applied to afferent fibers. Note the transient suppression of EP during propagation of spreading depression. (Modified from Gorji A. Spreading depression: a review of the clinical relevance. *Brain Res Brain Res Rev.* 2001;38:33.)

the induction of long-term potentiation in the neocortex (49). The prodromal excitation as well as late hyperexcitability is manifested in appearance of a burst of multiple action potentials and intense synaptic noise representing synchronized firing of neurons. The widely spread synchronization seems best explained by electrical continuity that could be provided by gap junctions. Patent gap junctions may provide a pathway not only for electric currents and ions, but also for intracellular “second” messengers and other active ingredients in cytosol (47).

SD is associated with transient, but major, localized redistributions of ions between the extra- and intracellular spaces. The $[K^+]_o$ rapidly rises and can reach levels as high as 40 to 80 mmol/L. This causes neuronal excitation followed by depolarization and a period of electrical silence during which the DC potential at the brain surface falls. Increases in $[K^+]_o$ could result

from a depolarization of both presynaptic and postsynaptic processes. In addition, presynaptic depolarization evokes Ca^{2+} -dependent synaptic transmission and glutamate release. The latter in turn enhances depolarization of postsynaptic elements and causes further increases in $[K^+]_o$. In addition to potassium and proton release from the cells, sodium, calcium, and chloride enter together with water causing cells to swell and the volume of the extracellular compartment to be decreased. SD is accompanied by an increase of glucose utilization and O_2 consumption. Recovery of SD depends on energy metabolism (50,51).

SD can be initiated by different stimuli. The most common model of SD initiation is KCl application to the neuronal tissues. Other methods of SD induction include mechanical, electrical, and thermal stimulations, application of the excitatory amino acids such as glutamate and aspartate, the Na^+-K^+ ATPase inhibitor ouabain, and metabolic inhibitors such as NaCN (52). The ionic processes responsible for the generation of SD are complex. Several ionic currents are involved; both high $[K^+]_o$ and low $[Ca^{2+}]_o$ can support either SD or epileptiform discharges depending on the state of the various membrane ion channels. Insight into the interplay of these different factors can best be obtained by the study of computer models solidly based on biophysical data. Thus, the model of Kager et al. (2008) revealed how the ignition of SD can result from the shift in the balance between slowly inactivating (persistent) inward and outward currents in apical dendrites of pyramidal cells in favor of the former. The effects of hypoxia and anoxia, through changes in Na/K pump and glial buffering, can also be put in evidence with these models (53,54).

Processes similar to SD in animal and human neocortex observed in experimental studies are thought to take place in a number of pathologic conditions in humans. SD belongs to the domain of the pathophysiology of the brain, and there are reasons to believe that it is involved in different clinical disorders, including migraine, cerebrovascular diseases, head injury, spinal cord disorders, epilepsy, and transient global amnesia (50). SD can alter the neurochemistry of cortical and subcortical structures, modulating oxygen distribution, cell survival in these structures, and behavior. Direct alterations of electrical activity of cortical neurons by the locally spreading wave can lead to clinical symptoms (e.g., the aura phase of migraine). The most common symptoms in the aura phase are visual, arising from dysfunction of occipital lobe neurons. The positive (excitatory) neurologic symptoms, for example, flashing lights, are usually followed by negative (suppressive) ones, for example, scotoma or hemianopia, in this phase. Subdural recordings in patients demonstrated that SD is critically involved in various disorders associated with acute neuronal injury including traumatic and spontaneous intracerebral hemorrhage (55).

CORTICAL FIELD POTENTIALS DURING GAS TENSION CHANGES IN TISSUE

This section deals with the alterations of epicortical field potentials and concomitant changes of the membrane potentials caused by deviations of the gas tension in brain tissue. Such changes of the gas tension may occur when, for instance, the

pulmonary and circulatory function is disturbed or when the local cerebral blood flow is inadequate.

First, the alterations of epicortical field potentials during selective hypercapnia are discussed; then, those associated with primary asphyxia are considered. It is shown that EEG changes may be similar under both conditions. The cortical DC potential, however, shows typical shifts that permit inferences concerning the cause of the accompanying EEG changes. The discussion of the effects of gas tension alterations on the bioelectrical activity of the CNS is based, again, on data derived from experimental work in animals.

Hypercapnia

If the CO_2 tension in the brain tissue is increased in a selective manner, typical reactions of the cortical field potentials as well as of the membrane potential and the postsynaptic potentials of individual neurons are found. These findings are shown in a summarized schematic view in Figure 2.17.

The animal experiments on which Figure 2.17 is based were carried out with the use of the so-called apnea technique. With this technique, interference of the effects of hypercapnia with simultaneous effects of hypoxia could be avoided. According to this technique, the experimental animal is ventilated for at least a half hour with pure oxygen. Thereafter, artificial ventilation is discontinued while the trachea of the animal remains connected with the O_2 reservoir. Under these conditions, the CO_2 tension progressively rises in the tissue for about 15 minutes without a concomitant fall of the oxygen tension below the baseline level.

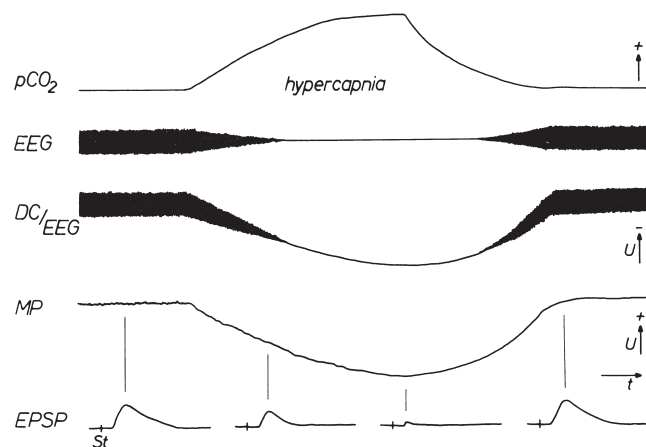


Figure 2.17 Effects of an isolated hypercapnia on epicortical field potentials (EEG, DC/EEG) and on membrane potential (MP). With increasing pCO_2 , the EEG disappears even if the pO_2 is above normal levels. The disappearance of the EEG is associated with a positive DC shift and a hyperpolarization of most of the neurons. Simultaneously, the amplitudes of stimulus (St) evoked EPSP are markedly reduced. (From original tracings from Speckmann EJ, Caspers, H. The effect of O_2 and CO_2 tensions in the nervous tissue on neuronal activity and DC potentials. In: Remond A, ed-in-chief. *Handbook of Electroencephalography and Clinical Neurophysiology*. Vol 2. Part C. Amsterdam: Elsevier; 1974:71–89.)

With isolated increment of the CO_2 tension in the cerebral tissue by means of the apnea technique, the amplitude of the conventional EEG decreases progressively. This amplitude reduction affects first the waves of higher frequency and then those of lower frequency. Prior to the extinction of normal EEG activity, there is once again a phase characterized by high-frequency EEG activity in the range of 50 to 70 Hz (1,56). The extinction of the EEG is associated with a shift of the DC potential in a positive direction. If the CO_2 tension is then lowered again by reventilation, the EEG waves return in the original spectral composition after a short latency. At the same time, the positive DC shift resolves (Fig. 2.17). Experiments in animals have shown that, with reduction of the pCO_2 , the EEG returns to normal activity even though the hypercapnia-induced suppression lasted for 1 hour or more. In these cases, a positive DC deflection of monophasic character was found to occur during the whole period of apnea (32,56,57).

Under the aforementioned conditions, the recording of the membrane potential of a cortical nerve cell shows a hyperpolarization while the CO_2 tension is increased. Extensive experimental studies in animals have demonstrated that such a hyperpolarization is caused primarily by a reduction of the EPSP (Fig. 2.17; also see Ref. 57). Consideration of field potentials, membrane potentials, and EPSP shows that epicortical DC potentials reflect neuronal hyperpolarization. The disappearance of the EEG waves is presumed to be caused mainly by the reduction of postsynaptic activity.

Asphyxia

Primary asphyxia exemplified by respiratory arrest after air ventilation is associated with combined CNS effects of hypercapnia and hypoxia. The effects of gas tension changes on the field potentials and on the membrane potential of individual neurons are schematically shown in Figure 2.18. In the corresponding animal experiments, the artificial ventilation with air was either temporarily (Fig. 2.18A) or persistently (Fig. 2.18B) interrupted.

With such an interruption of artificial ventilation with air, the conventional EEG waves disappear within less than 1 minute. This process is accompanied by a negative DC potential shift from the baseline, which has been characterized as *initial negativity* (1 in Fig. 2.18). While the EEG shows an isoelectric line in the further course of asphyxia, additional potential shifts are detectable with DC recording technique. The initial negativity is followed by a positive DC shift termed *intermediate positivity* (2 in Fig. 2.18). If reventilation is performed in this phase of asphyxia, an additional positive DC shift is observed, appropriately termed *reactive positivity* (3 in Fig. 2.18A). According to the analysis of the experimental work, the intermediate and the reactive types of positivity are due to an increase of CO_2 tension in the brain tissue. With the resolution of the reactive positivity, a restitution of the fast field potentials occurs that is also demonstrable with the conventional EEG. A comparison of the DC shifts and the alterations of the membrane potentials shows a parallelism of both events (1,13,14,32,56,57).

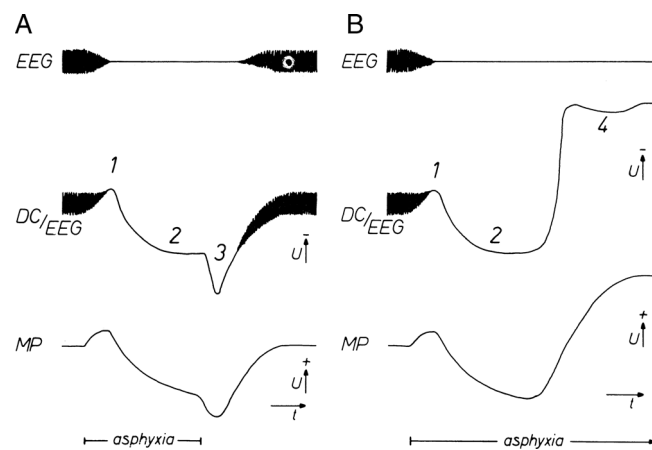


Figure 2.18 Alterations of EEG, DC/EEG, and neuronal membrane potential (MP) during primary asphyxia. **A:** The abolition and the reappearance of EEG during a transient asphyxia goes in parallel with typical DC shifts: (1) initial negativity, (2) intermediate positivity, and (3) reactive positivity. These DC fluctuations are accompanied by corresponding reactions of the MP. **B:** With continuing asphyxia, the EEG remains abolished and the intermediate positivity (2) turns over into a terminal negativity (4). The latter DC negativity corresponds to a breakdown of neuronal membrane potential. (From original tracings from Speckmann EJ, Caspers H. The effect of O₂ and CO₂ tensions in the nervous tissue on neuronal activity and DC potentials. In: Remond A, ed-in-chief. *Handbook of Electroencephalography and Clinical Neurophysiology*. Vol 2. Part C. Amsterdam: Elsevier; 1974:71–89.)

If the interruption of the artificial ventilation is continued for a longer period of time, then the intermediate positivity converts into the so-called terminal negativity (4 in Fig. 2.18B). This negative DC shift correlates with the breakdown of the neuronal membrane potential. The terminal effects are due to a critical lack of oxygen. The terminal negativity may be reversible for a substantial period of time under certain experimental conditions if the artificial ventilation is resumed and the reduction of the cerebral circulation is counteracted with circulation support measures (57).

In summary, a comparison of EEG and DC potentials in selective hypercapnia and primary asphyxia shows that the recording of cortical field potentials with DC amplifiers provides a more accurate picture of the actual functional state of nerve cells.

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