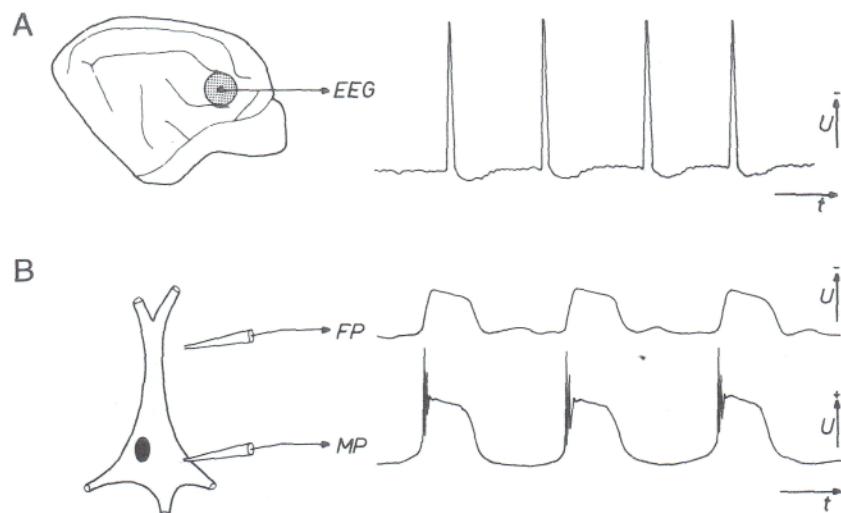


Figure 2.9. EEG (A) and membrane potential (MP) changes of a pyramidal tract neuron and extracellular field potential (FP) recorded in the vicinity of the impaled neuron (B) during focal interictal activity elicited by application of penicillin to the cortical surface (hatched area in A). Drawings of 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.

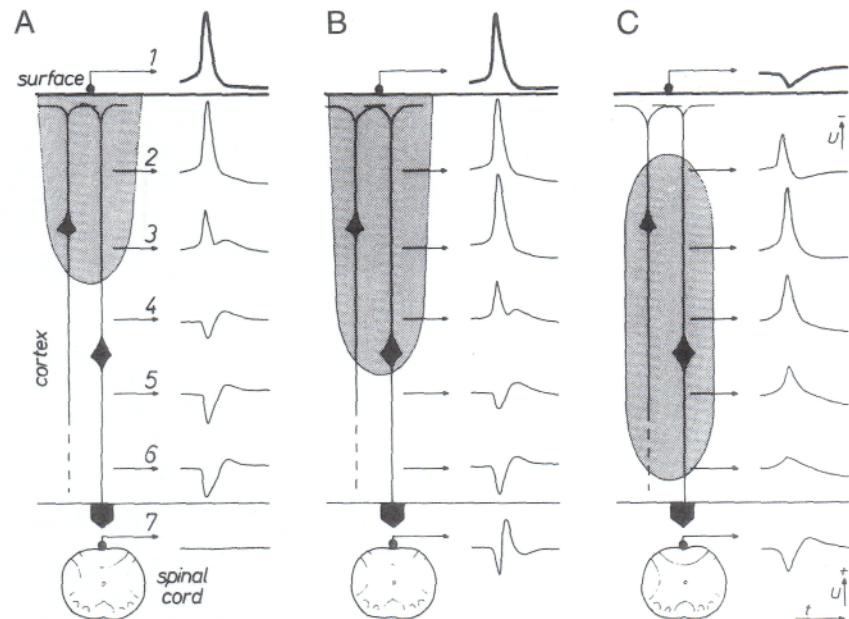


carried out from the cortical surface, from inside the cortex, and from the spinal cord. The spinal field potentials permit the observation of electrical activity descending from the cortex to the spinal cord. In Fig. 2.10A, negative field potentials are recorded from the cortical surface and from the 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 through 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. 2.9), then it must also be assumed that deeper cortical elements are involved in convulsive activity shown in Fig.

2.10B in contrast with Fig. 2.10A. 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 Fig. 2.10B. If one compares the recordings in Fig. 2.10A and Fig. 2.10B, 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 (Elger and Speckmann, 1980, 1983; Elger et al., 1981; also see Gumnit, 1974; Petsche et al., 1981; Speckmann and Elger, 1983; Wieser, 1983).

If penicillin is applied to deeper cortical laminae (Fig. 2.10C), then negative field potentials will be confined to that region. These potentials are consistently accompanied by descending activity to the spinal cord. Under these condi-

Figure 2.10. Cortical field potentials recorded at the surface (1) and from within the cortex (2–6) 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 intracortical 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 μm . (From original tracings from Elger, C.E., Speckmann, E.J., Caspers, H., et al. 1981. Focal interictal epileptiform discharges in the cortex of the rat: laminar restriction and its consequences for activity descending to the spinal cord. In *Physiology and Pharmacology of Epileptogenic Phenomena*, Eds. M.R. Klee, H.D. Lux, and E.J. Speckmann. New York: Raven Press.)



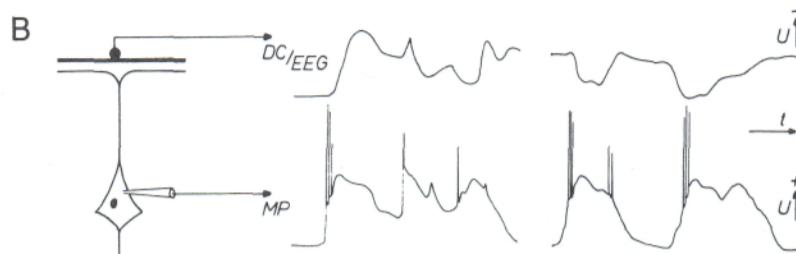
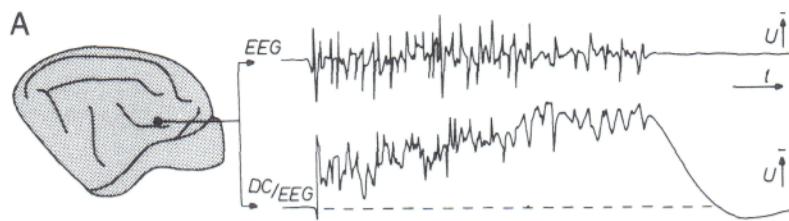


Figure 2.11. Simultaneous recordings of EEG and DC/EEG (**A**) and of DC/EEG and membrane potential (MP) of a pyramidal tract neuron (**B**) during generalized tonic-clonic seizures elicited by pentylenetetrazol. (Drawings after original tracings from experiments in the cat's motor cortex. The sweep speed in **B** is 10 times that in **A**.)

tions, there is frequently nothing but a positive potential fluctuation of minor amplitude at the cortical surface (Elger and Speckmann, 1983; Elger et al., 1981).

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 Purpura et al., 1972; Speckmann, 1986).

Figure 2.11A 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 (Caspers and Speckmann, 1969; Caspers et al., 1980, 1984; Gumnit, 1974; Speckmann, 1986; Speckmann and Caspers, 1979b; Speckmann and Elger, 1984).

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. 2.11B). If these PDSs are correlated with the potential fluctuations in the DC recording, it can be noticed that the PDS 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) (Speckmann et al., 1978; Speckmann and Caspers, 1979a,b).

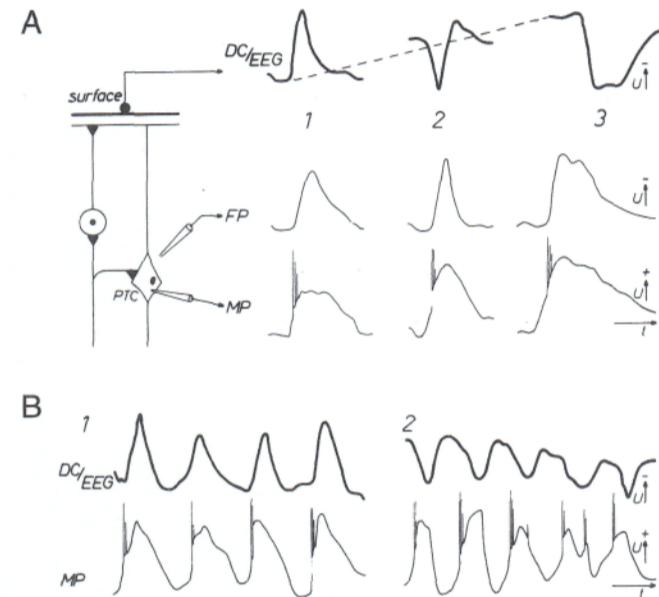


Figure 2.12. Single potential fluctuations at the cortical surface (DC/EEG) and concomitant membrane potential (MP) of a pyramidal tract cell (PTC) and field potentials (FP) in the PTC layer during generalized tonic-clonic seizures. The seizure activity was induced by pentylenetetrazol. **A:** The negative 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*, *2*). (From original tracings from Speckmann, E.J., Caspers, H., and Jansen, R.W.C. 1978. Laminar distribution of cortical field potentials in relation to neuronal field activities during seizure discharges. In *Architectonics of the Cerebral Cortex*. IBRO Monograph Series, vol. 3, Eds. M.A.B. Brazier and H. Petsche, pp. 191–209. New York: Raven Press.)

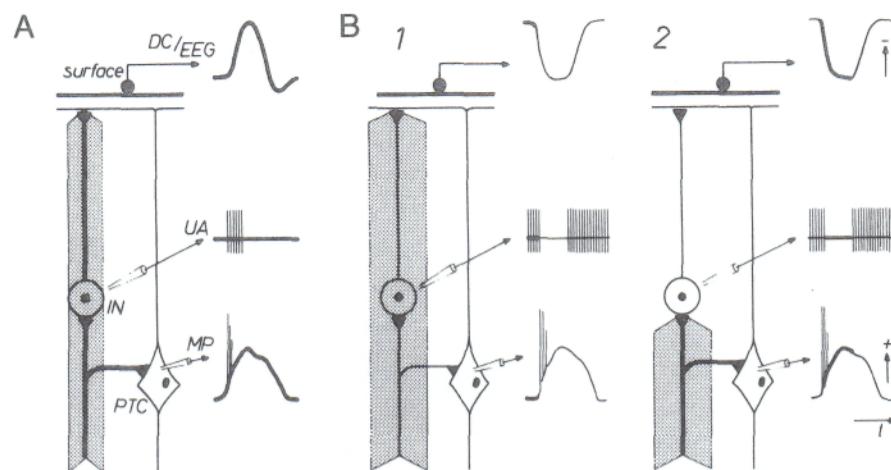


Figure 2.13. Flow charts of neuronal processes possibly responsible for the generation of DC/EEG waves of opposite polarity during a generalized tonic-clonic seizure. Hatched arrows, symbols for continuous asynchronous input to the cortex; heavy lines, symbols for phasic volleys giving rise to single 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 disinhibition of the upper neuronal structures and therewith to a positive fluctuation of the superficial DC/EEG potential (2). (From original tracings from Speckmann, E.J., Caspers, H., and Jansen, R.W.C. 1978. Laminar distribution of cortical fluid potentials in relation to neuronal field activities during seizure discharges. In *Architectonics of the Cerebral Cortex*. IBRO Monograph Series, vol. 3, Eds. M.A.B. Brazier and H. Petsche, pp. 191–209. New York: Raven Press.)

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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. 20.12A). These stereotyped potential fluctuations in deep cortical layers correspond with field potentials at the cortical surface with either monophasic negative or positive (Fig. 20.12A1,3) or with polyphasic (Fig. 20.12A2) configurations. This statement does not merely apply to individual ictal potentials but is also true for prolonged trains of potentials during the convolution. As Fig. 20.12B 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 convolution (also see Fig. 20.12A), 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 when the negative DC shift at the cortical surface reaches and exceeds a critical value (Speckmann and Caspers, 1979a,b; Speckmann et al., 1972, 1978).

These data are interpreted with flow charts in Fig. 20.13. 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 Fig. 20.13. Accordingly, the afferent influx in Fig. 20.13A is smaller than that in Fig. 20.13B. Therefore, there is a smaller DC shift in Fig. 20.13A and a prominent one in Fig. 20.13B. In

the case of Fig. 20.13A, a synchronized inflow of impulses from subcortical 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 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. 20.13B). If an additional highly synchronized afferent inflow 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 disinhibition 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 (Speckmann et al., 1978; Speckmann and Caspers, 1979b).

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 Fig. 2.14.

The animal experiments on which Fig. 2.14 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.

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 (Caspers et al., 1979; Speckmann and Caspers, 1979a).

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. 2.14). 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 (Caspers and Speckmann, 1974; Caspers et al., 1979; Speckmann and Caspers, 1974).

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. 2.14; also see Speckmann and Caspers, 1974). Consideration of field potentials, of membrane potentials, and of 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 Fig. 2.15. In the corresponding animal experiments, the artificial ventilation with air was either temporarily (Fig. 2.15A) or persistently (Fig. 2.15B) 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. 2.15). While the EEG shows

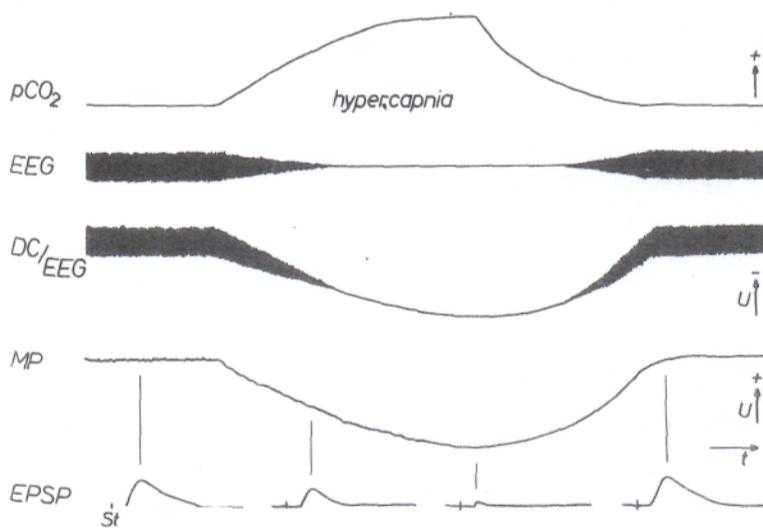
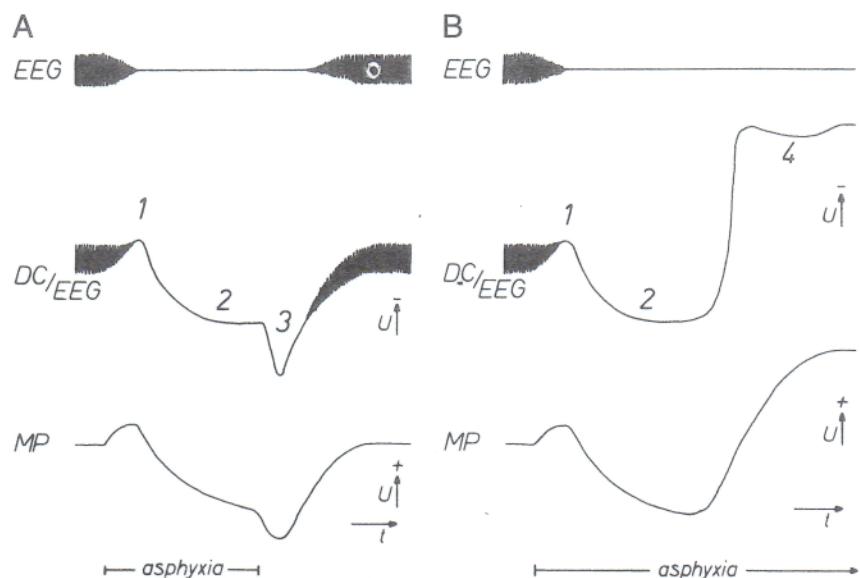


Figure 2.14. Effects of an isolated hypercapnia on epicortical field potentials (EEG, DC/EEG) and on membrane potential (MP). With increasing $p\text{CO}_2$, the EEG disappears even if the $p\text{O}_2$ is above normal levels. The disappearance of the EEG is associated with a positive DC shift and a hyperpolarization of most of the neurons. Simultaneously, the amplitudes of stimulus (St) evoked EPSP are markedly reduced. (From original tracings from Speckmann, E.J., and Caspers, H. 1974. The effect of O_2 and CO_2 tensions in the nervous tissue on neuronal activity and DC potentials. In *Handbook of Electroencephalography and Clinical Neurophysiology*, vol. 2, part C, Ed.-in-chief A. Remond, pp. 71–89. Amsterdam: Elsevier.)

Figure 2.15. 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, (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, E.J., and Caspers, H. 1974. The effect of O_2 and CO_2 tensions in the nervous tissue on neuronal activity and DC potentials. In *Handbook of Electroencephalography and Clinical Neurophysiology*, vol. 2, part C, Ed.-in-chief A. Remond, pp. 71–89. Amsterdam: Elsevier.)



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. 2.15A). If reventilation is performed in this phase of asphyxia, an additional positive DC shift is observed, appropriately termed *reactive positivity* (3 in Fig. 2.15A). 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 (Caspers and Speckmann, 1974; Caspers et al., 1979, 1980, 1984; Speckmann and Caspers, 1974, 1979a).

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. 2.15B). 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 (Speckmann and Caspers, 1974).

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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