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THE NEURAL SEMICONDUCTION CONTROL SYSTEM AND ITS INTERACTION WITH APPLIED ELECTRICAL CURRENT AND MAGNETIC FIELDS* **

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The existence of measurable direct current potentials across portions of the amphibian brain was first reported by Gerard and Libet (1940). Similar findings were reported in the human by Goldring *et al.* (1950) and most recently Aladjalova (1964) has published a comprehensive review of this phenomena. Studies in this laboratory of the total direct current (d.c.) pattern and its relationship to the entire central nervous system have led us to postulate that these potentials represent an organized data transmission and control system dealing with very primitive modalities (Becker, 1960; Becker *et al.*, 1962). The potentials are maintained at constant or slowly varying amplitudes for long periods of time; in the normal preparation it is conceivable that they may be maintained by a constant low amplitude current flow (Becker *et al.*, 1962a). Direct measurements of the postulated current flow have been technically impossible to make for a variety of reasons. However, indirect evidence has been obtained for such a current, i.e., Hall voltages have been observed in amphibians and directly related to the physiological state of the peripheral nerves (Becker, 1961a). Additional observations have been reported indicating that the postulated current flow had certain semiconducting characteristics (Becker, 1962). In a wide variety of animals from flatworms to man, similar d.c. potentials have been found to show a consistent pattern and to be associated with a variety of basic neurophysiological functions (Becker, 1961b; 1963). In all cases a specific d.c. vector has been observed in the cranial area. This vector is located in the midline and is directed in a fronto-occipitally direction with the frontal or anterior area normally being negative with respect to the occipital. A very high degree of synchronization has been observed between the magnitude of this electrical vector and the levels of consciousness of the organism. In the human, sleep, hypnosis and general anesthesia have all been associated with a decrease in the vector magnitude, the amount of decrease being roughly proportional to the depth of the loss of consciousness as clinically determined (Friedman *et al.*, 1962). It is postulated that the source of this vector resides in an organized d.c. semiconducting system (Fig. 1) within median unpaired structures in the brain stem and that it represents a regulatory system governing the levels of irritability of higher cerebral centers.

Based on this concept, one may make several predictions, all suitable for experimental verification.

a. The application of low amperage direct current along the midline cephalic vector with a polarity opposing that normally found, should produce some evidence of decreasing cerebral irritability (consciousness).

b. Application of a similar current but with a polarity adding to that normally found

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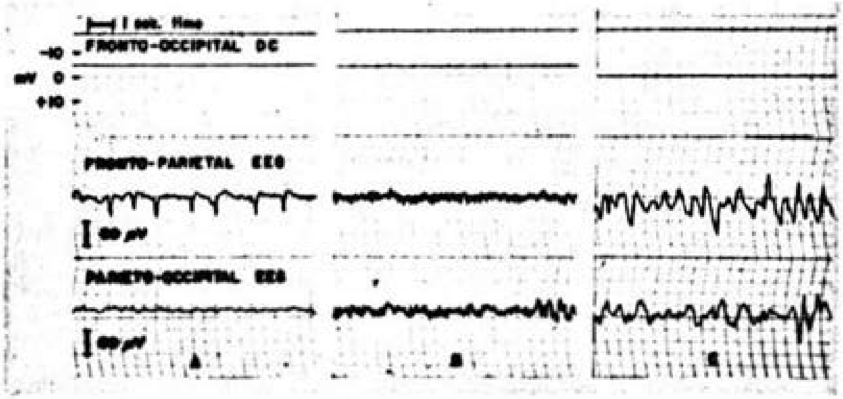

Fig. 1. Changes in the human fronto-occipital d.c. potential and electroencephalogram with general anesthesia. Section A demonstrates the pattern present at the start of anesthesia, the d.c. level is 5mV frontally-negative. Section B was taken ten minutes after 10 ml of 2.5% pentothal were administered intravenously. It demonstrates a 1 mV decrease in the d.c. potential and a fast EEG pattern typical of barbiturate effect. Section C was taken fifteen minutes after 500 ml/min. of cyclopropane was starte in a semi-closed system. Clinically, the patient was in deep general anesthesia. The fronto-occipital d has dropped to zero, and both channels of EEG demonstrate a marked delta pattern.

should increase the level of cerebral irritability. It may be possible, in this case, to overcome or reverse several of the depressant effects of general anesthetic agents.

c. Since the naturally occurring d.c. potentials have been observed to show a specific modulation frequency band (0.1 to 1 c.p.s.) during periods of changing levels of consciousness it is predicted that the addition of similar modulation frequencies would potentiate the effects of the administered direct currents.

d. Application of similar levels of direct current across vectors other than the midline fronto-occipital should have little or no physiological effect.

e. It should be possible to observe an interaction between the midline d.c. vector and an external static magnetic field applied at right angles to the vector axis, provided the magnetic field strength was sufficient and the charge carriers of the direct current possessed sufficient mobility. Under these circumstances it is predicted that the interaction would result in the deviation of an appreciable number of charge carriers into alternate (possibly higher resistance) pathways, resulting in a decrease in the total vector current. It should, therefore, be possible to produce evidence of a decrease in the level of cerebral irritability with sufficiently high strength magnetic fields applied in this fashion. However, in contradistinction to the application of direct current, the converse should not be possible, i.e., no method of external static magnetic field application would result in an increase in levels of irritability. This latter effect obviously requires the addition of electrical energy to the vector system by charge carrier injection.

Methods

Techniques and instrumentation used in the measurement of the normally occurring direct current potentials of living organisms are described in full in the previous series of publications (Becker, 1960, 1961a, b, 1962a, b, 1963; Friedman *et al.*, 1962).

In the present study electrical currents and magnetic fields were administered to amphibians only. Tranquilization necessary for experimentation was obtained with Tr caine (Sandoz). Electrical current was obtained from dry cell batteries through a prec sion resistor network and monitored with a Hewlett-Packard 425-A micro-ammeter. Modulation frequencies were obtained from a Hewlett-Packard 202-A low frequency function generator and capacity coupled to the direct current to produce 25% modulation amplitude. Electrodes for current administration were Ag-AgCl with salt bridges. Magnetic fields were obtained from a Varian 6" electromagnet model V-4007-1 with ring shim pole caps, producing excellent field uniformity. Field strengths were measured with a Varian F-8 nuclear magnetic resonance flux meter using a proton probe. For magnetic field exposures the lightly tranquilized animal was placed on a sheet of plexiglass, suspended in the magnet gap with its head occupying the area of maximum field uniformity with the long axis (fronto-occipital) of the head carefully positioned at 90° to the flux lines of the field. EEG electrodes (Ag-AgCl) were positioned and held in place with non-magnetic clamps. Magnet gap diameter permitted positioning of only one pair of electrodes at a time. The magnetic field strength was continuously variable and field strengths were increased and decreased in uniform fashion, with no sudden changes in strength. No external modulation was added to the field; the power supply delivered ripple-free current to the magnet coils. Particularly, the field was totally free of fluctuations in the 1 to 30 c.p.s. frequency ranges, which could have been confused with EEG patterns.

Results

a. Administration of direct current to oppose the normal fronto-occipital d.c. potential in lightly tranquilized animals (Fig. 2 upper section).

As the direct current is increased in magnitude, a delta wave pattern becomes evident on the EEG at 30 μA. Further increases in the current produce correspondingly increased amplitude in the delta waves. This effect is visible in both channels of EEG recordings, but is more prominent in the fore-to-midbrain channel. Both channels, however, demonstrate a marked change from the predominantly alpha pattern seen before

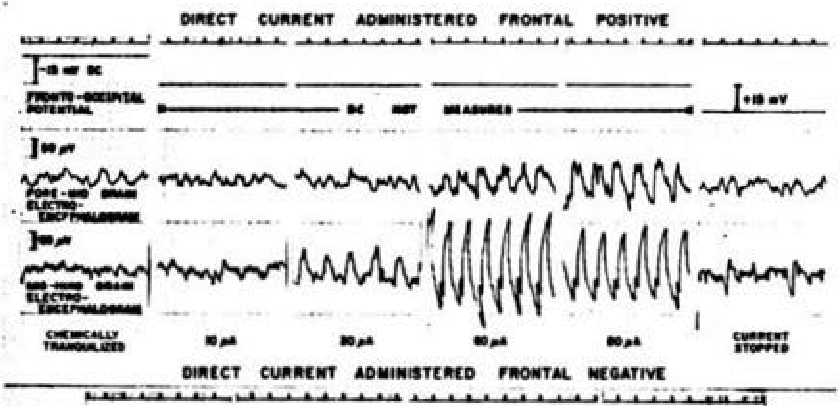

Fig. 2. The effect of administration of direct current (midline, cephalocaudally) to amphibia. The upper section illustrates the changes produced by various amounts of frontally-positive current administered to a lightly tranquilized animal.

The lower section of recordings similarly demonstrates the effects of administering current in a frontally-negative fashion to a deeply anesthetized animal exhibiting zero d.c. potential, delta wave EEG patterns, and depression of respiratory movements.

In both series of recordings the upper time marker has a one/second frequency, and amplification levels of the three channels are as noted.

current administration. Accompanying these EEG signs indicative of deepening loss of consciousness is a depression of the respiratory center, respiration ceasing generally between 80 and 100 μA. After completion of the experiment, measurements of the fronto-occipital d.c. potential show a reversal of the pattern seen prior to the current administration with what appears to be a residual polarization induced by the current flow. This persists some 15 to 20 minutes, gradually decreasing to zero, and then returning to the normal frontal-negative pattern. The time to full recovery from the effects of the tranquilizing dose of Tricaine is greatly lengthened. Normal recovery time is 20 minutes following removal from solution. If current is administered with a frontal-positive polarity for 10 to 20 minutes after removal from solution, recovery is delayed until 30 to 40 minutes following cessation of current administration.

b. Administration of direct current oriented to produce a normal d.c. potential in deeply anesthetized animals (Fig. 2 lower section).

The conditions prior to current administration were a fronto-occipital d.c. potential of almost zero, delta patterns in both channels of the EEG, and absence of respiratory movements. The administration of 170 μA of frontally negative direct current results in the

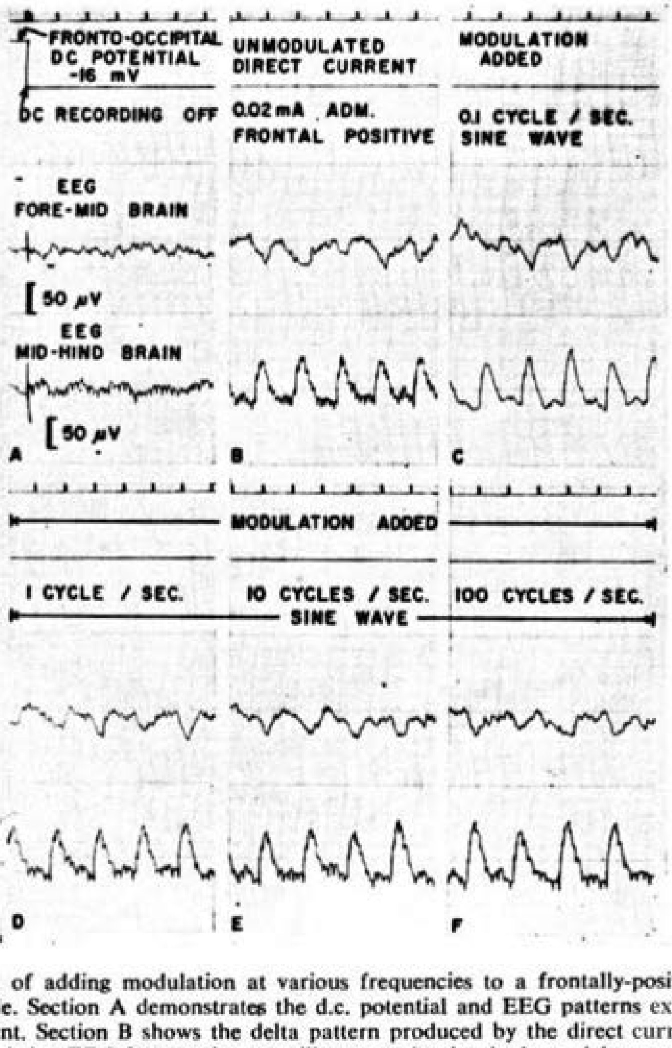

Fig. 3. The effect of adding modulation at various frequencies to a frontally-positive direct current of 20 μA magnitude. Section A demonstrates the d.c. potential and EEG patterns existing before starting the direct current. Section B shows the delta pattern produced by the direct current passage alone. Note that the pre-existing EEG frequencies are still present despite the large delta waves.

The remaining sections indicate the varying degree of obliteration of alpha pattern by various modulation frequencies.

appearance of a fairly typical alpha pattern in the fore-to-midbrain channel, this however, being accompanied by an increase in the mid-to-hindbrain delta activity. However, respiratory movements return with normal rate and rhythm during the time that this amount of current is administered and with cessation of current flow, the respiratory movements cease. We have not been successful in restoring responses to painful stimuli, and it is evident that somewhat higher levels of current must be administered to produce even the minimal changes seen in the figure. The general effect of frontally-negative current administered to a deeply anesthetized animal, however, is some apparent lightening of the depth of anesthesia.

The differential nature of the results obtained in experiments a and b, depending only upon the polarity of the administered currents, indicates that the results are not due to secondary effects, such as pain or heating at electrode junctions, but are dependent upon the direction of current passage. Other experiments using similar levels of direct current administered transversely across the head have failed to demonstrate any such specificity of action, although delta frequencies are occasionally produced in the EEG of lightly tranquilized animals with 50–60 μA of current so oriented.

c. Administration of modulated direct currents to lightly tranquilized animals (Fig. 3).

The production of EEG patterns typical of deep anesthesia by passing frontally-positive direct current appeared to substantiate claims for the production of clinical anesthesia by similarly oriented, but modulated, direct current (Anan'ev *et al.*, 1960). The modulation utilized is generally a sine wave of 100 c.p.s. superimposed upon the direct current, although the choice of this frequency is strictly empirical. Since it is impossible to record EEG patterns during the passage of the modulated current, electroen-

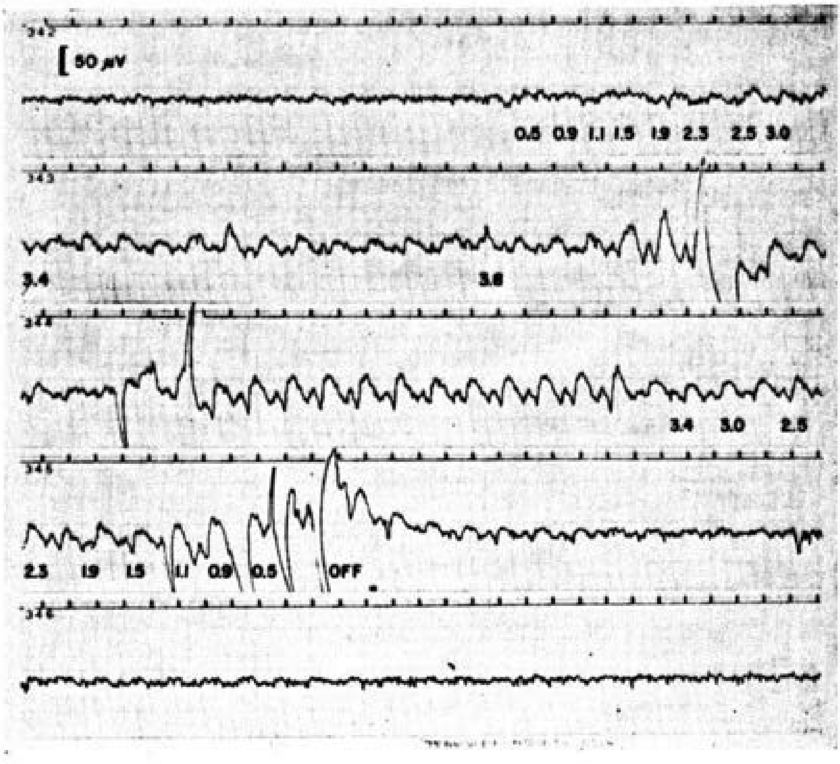

Fig. 4. Alteration in electroencephalogram pattern of a lightly tranquilized amphibian produced by exposure to a uniform steady-state transverse magnetic field. The five recordings, arranged vertically, were taken sequentially, the time markers in all being one/second and the EEG being recorded from the fore-to-midbrain area. In the uppermost recording, the EEG before the magnetic field was applied is shown demonstrating an alpha frequency of 10–12 c.p.s. The numbers to the right in this record are the field strengths of the magnetic field in kilogauss as it is turned on and increased.

cephalographic confirmation of the anesthetic state has not been obtained by workers in the field of electronarcosis. In our experiments, a sufficient amount of direct current was passed in a frontally-positive direction to produce delta patterns in the EEG. Various modulation frequencies were then added to this basic current, and EEG recordings made within five seconds of the cessation of each modulation frequency, the basic d.c. level being maintained throughout. Marked potentiation of the EEG effect was obtained by a modulating frequency of 0.1 c.p.s., with less effect produced by higher frequencies. The neural direct current system, therefore, does appear to be frequency-sensitive, particularly in the ultra-low frequency range.

d. Exposure of lightly tranquilized animals to transverse magnetic fields (Fig. 4).

In the lightly tranquilized animal, the alpha pattern EEG persists during exposure to low values of magnetic field (below 3 kilogauss), regardless of the length of time of exposure. If the field strength is increased over 3 kilogauss, delta patterns become evident in the EEG, and at 3.8 kilogauss they become persistent. Increase in field strength over this value (to a maximum of 5 kilogauss) does not result in an increase in magnitude of the delta pattern, or any other alterations in the EEG. Decrease of the field to values below 3 kilogauss (or to zero) results in a prompt return of the EEG to the pre-existing alpha pattern. There is thus no residual polarization effect as is present afte administration of frontally-positive electrical current. Recordings of fronto-occipital d.c. potentials during the same type of experiment show a prompt (10 sec) decrease in the pre-existing negative polarity as the field is applied, that is roughly dependent upon the field strength utilized and synchronous with the EEG changes. Deviation of the long axis of the head from its position transverse (90°) to the flux lines of the magnetic field decreases both effects. While only rough estimates have been made, it appears that positions greater than 20° from the transverse are ineffective in producing the phenomenon. As predicted, no alteration of EEG patterns or any change in any physiological variable was noted during exposure of a deeply anesthetized animal to similar magnetic fields. Technical difficulties prevented the evaluation of magnetic fields modulated at the same frequencies as in the applied current experiments. Theoretically, at least, a potentiation of the effect should be produced.

Discussions and conclusions

In amphibians the application of either midline fronto-occipital direct electrical current or transverse static magnetic fields results in changes in the electroencephalographic pattern with parallel changes in behavioral patterns indicating alterations in the level of consciousness. The observed effects were in agreement with those predicted on the theory of the neural direct current potentials constituting a control system governing, in part, the general level of cerebral irritability. It would appear that this is probably the mechanism involved in the production of electronarcosis by the method of Aran'ev (1960). Furthermore, it is not unlikely that the basic action of all general anesthetic agents, regardless of their physiochemical activity (Pauling, 1961), is to interfere with the action of this system.

The experimental conditions and results of this study are somewhat different from those reported by Kholodov (1964). While he found EEG evidence of "inhibition" (spindles and slow waves) somewhat similar to ours, he apparently made no attempt to maintain a specific vectorial relationship between the magnetic field and the cephalic axis of the animal. In addition, in one study the "encéphale isolé" preparation was used. Our studies on the d.c. system had previously demonstrated major alterations in the pattern and polarity following high cord transection and, therefore, such a preparation was considered unsuitable for any investigation of the interaction between the d.c. system and magnetic fields. It is suggested that some of the effects noted by Kholodov might have been the results of currents induced by sudden changes in the field. In the series of experiments reported here, we attempted to avoid the possible physiological effects of such currents by changing the field strength slowly.

It would appear unlikely that sufficient interaction could be developed between an strated physiological changes. In addition, Liberman *et al.* (1959) have previously shown no effect of higher strength magnetic fields on action potential activity. However, the interaction between an applied magnetic field and a current composed of highly mobile charge carriers is known to be many orders of magnitude greater than the interaction with an ionic current of the same magnitude. Szent-Gyorgyi (1960) has long proposed semiconduction properties for biological systems as possible answers to the difficult problems of energy conversion. Therefore, as a conceptual framework for further investigation it is proposed that the basis of the neural direct current system is the movement of mobile charge carriers within some solid state matrix in the neurone. Semiconduction systems have been previously described in the chloroplast by Calvin and Androes (1962), and more recently in bone by our group (Becker *et al.*, 1964). In the latter instance it has been possible to describe the type of semiconduction matrix (multiple PN junction diodes) in considerable detail (Becker, 1965).

The results described in this paper satisfy in all details the five effects predicted on the theory of a semiconducting nature to the cephalic vector portion of the direct current neural system. It is evident that the electronic nature of this system renders it susceptible to alteration by externally generated electrical currents or magnetic fields provided they are of appropriate magnitude and orientation. Such alterations may be clinically desirable under certain circumstances.

REFERENCES

ALADJALOVA, N. A. (1964): *Slow Electrical Processes in the Brain.* Elsevier Publishing Co., New York.

ANAN'EV, M. G. *et al.* (1960): Preliminary data on experimental electronarcosis. English translation in *Anesthesiology, 21,* 215.

BECKER, R. O. (1960): The bioelectric field pattern in the salamander and its simulation by an electronic analog. *IRE Transactions on Medical Electronics, 7,* 202.

BECKER, R. O. (1961a): Search for evidence of axial current flow in peripheral nerves of salamander. *Science, 134,* 101.

BECKER, R. O. (1961b): The bioelectric factors in amphibian limb regeneration. *J. Bone Jt Surg., 43A,* 643.

BECKER, R. O. (1962): Some observations indicating the possibility of longitudinal charge-carrier flow in the peripheral nerves. In: *Biological Prototypes and Synthetic Systems,* p. 1, E. E. Bernard and M. R. Kare, Editors. Plenum Press, New York.

BECKER, R. O., BACHMAN, C. H. and SLAUGHTER, W. (1962a): The longitudinal direct current gradients of spinal nerves. *Nature (Lond.), 196,* 675.

BECKER, R. O., BACHMAN, C. H. and FRIEDMAN, H. (1962b): The direct current control system. *N. Y. St. J. Med., 62,* 1169.

BECKER, R. O. (1963): The direct current field: A primitive control and communication system related to growth processes. *Proceedings of XVI International Congress of Zoology, Washington, D.C., Vol. 3,* p. 179.

BECKER, R. O., BASSETT, C. A. L. and BACHMAN, C. H. (1964): Bioelectric factors controlling bone growth. *Bone Biodynamics,* ed. Frost, H. M. Little Brown and Co.

BECKER, R. O. and BROWN, F. M. (1965): Photoelectric effects in human bone. *Nature (Lond.), 206,* 1325.

CALVIN, M. and ANDROES, G. M. (1962): Primary quantum conversion in photosynthesis. *Science, 138,* 867.

FRIEDMAN, H., BECKER, R. O. and BACHMAN, C. H. (1962): Direct current potentials in hypno-analgesia. *Arch. gen. Psychiat., 7,* 193.

GERARD, R. W. and LIBET, B. (1940): The control of normal and convulsive brain potentials. *Amer. J. Psychiat., 96,* 1125.

GOLDRING, S., ULETT, G., O'LEARY, J. L. and GREDITZES, A. (1950): Initial survey of slow potential changes obtained under resting conditions and incident to convulsive therapy. *Electroenceph. clin. Neurophysiol., 3,* 297.

KHOLODOV, YU. A. (1964): Effects on the central nervous system. In: *Biological Effects of Magnetic Fields,* ed. Barnothy, M. F. Plenum Press, New York.

LIBERMAN, E. A., VAINTSVAIG, M. N. and TAOFINA, L. M. (1959): The effect of a constant magnetic field on the excitation threshold of isolated frog nerves. *Biofizika, 4,* 505.

PAULING, L. (1961): A molecular theory of general anesthesia. *Science, 134,* 15.

SZENT-GYORGYI, A. (1960): *Introduction to a Submolecular Biology.* Academic Press, New York.