THE CHANGES IN THE ELECTRIC IMPEDANCE DURING ACTIVITY AND THE EFFECT OF ALKALOIDS AND POLARIZATION UPON THE BIOELECTRIC PROCESSES IN THE MYELINATED NERVE FIBRE

by

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In 1939, COLE AND CURTIS made alternating current impedance measurements on the fresh water plant Nitella and the giant axon of the squid during the passage of an impulse. In their experiments, the relationship between the membrane resistance and the electromotive force therein has been most impressively brought out. Hence a similar experiment on the myelinated nerve fibre seemed very desirable to us for a better understanding of the process of excitation in the plasma membrane at the node of RANVIER.

In the present work, the impedance of the single motor nerve fibre of the toad has been investigated by the use of the "bridge-insulator" method. This method of insulating an isolated single nerve fibre between two neighbouring nodes provides us with a simple but very direct way of demonstrating the remarkably close interrelationship between the impedance changes and the action current in this fibre. The effects of several alkaloids and electrotonic polarization upon the time course of the impedance changes have further been investigated in the hope of securing additional evidence that the impedance change and the production of action current are only two different expressions of one and the same process occurring at the plasma membrane of the node of RANVIER.

With a whole nerve trunk, LULLIES (1930) has already found a decrease in the impedance for bridge currents strong enough to excite the nerve fibres. But, as the effect is demonstrable with only low frequency alternating currents, its relationship with those presented in this paper is not very clear at present.

METHOD

Nerve fibres of above 11 microns in diameter have been selected for the experiments. The technique of isolating the fibres is fundamentally the same as that described previously (TASAKI, 1939), except that in the present investigation the operation was carried out under a binocular microscope. Care was taken to remove all the inactive fibres and tissues around the nerve fibre to be examined. The isolated region of the nerve fibre was mounted on a "bridge-insulator" consisting of two separate glass plates fixed at a distance (between the edges) of about 1 mm. In each of the pools of RINGER on both sides of the bridge-insulator, a non-polarizable electrode of the $Zn\text{-}ZnSO_4$-RINGER (agar) type was immersed.

The isolated region of the fibre on the bridge-insulator, together with the electrodes dipping into the pools, formed one arm of a Wheatstone bridge. The experimental arrangement used in the later stage of the present investigation is shown in Fig. 1. The resistance R in the figure was in most cases 1 megohm and r was generally between 0.3 and 3 ohms. The bridge was balanced by adjusting the condenser C and the resistance r continuously. The bridge input consisted of an alternating

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current (A.C.) from a beat-oscillator, its frequency being between 1 and 10 kilocycles per second (kc). As too strong an A.C. reduced the electric response of the nerve fibre, as already described by ROSENBLUETH (1940) and his coworkers care was taken not to allow its amplitude to exceed about 50 mV.

Most experiments were made at temperatures between 2 and 6° C. At such low temperatures the duration of the action current of the nerve fibre is several msec and this made it possible to demonstrate impedance changes with A.C. of relatively low frequencies. Moreover, cold raises the threshold of the fibre for brief currents and consequently permits us to increase the bridge input without appreciably affecting the excitability of the fibre. At 2° C, an A.C. of about 20 mV at 3 kc was found not to bring about any detectable change in the threshold of the fibre.

The nerve fibre was brought into action by means of an induction coil I or a battery B in the figure. The contacts in the primary circuit of the induction coil and in the battery circuit (K_1 and K_2) were operated with a HELMHOLTZ pendulum, of which another break contact was used to start single sweeps of the cathode ray oscillograph. The figures on the face of the oscillograph were photographed.

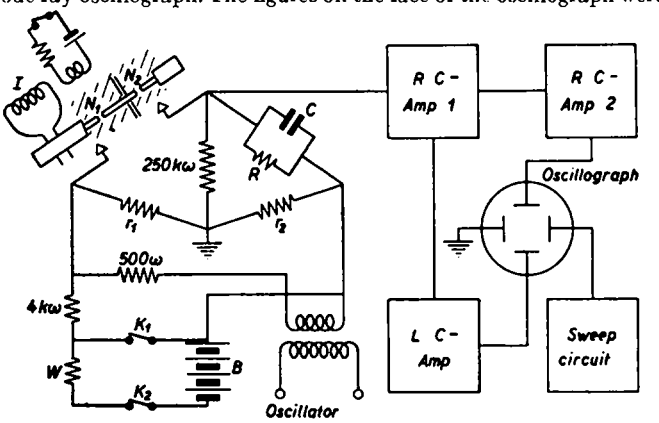

Fig. 1. Schematic diagram of the electrical equipment used for the impedance determinations during activity. The nerve fibre, of which two nodes of RANVIER N_1 and N_2 are exposed, is at the left of the bridge. R, r_1 and r_2 are respectively the resistances of the order of 1 megohm, 50 ohms and 1 ohm. C is the variable condenser (below 300 pF) and W the variable resistance used to control the strength of D.C. from the battery B of about 20 volts. The untuned resistance-capacity coupled amplifier and the tuned impedance amplifier are represented by RC-amp and LC-amp. K's are the knock-over keys of a HELMHOLTZ pendulum and I is the induction coil.

The bridge output was first connected to a 2-stage resistance-capacity coupled (RC-) amplifier and then to another RC-amplifier or to a transformer coupled (LC-) amplifier tuned to the frequency of the oscillator. In the experiments of Figs 5 and 6, the output of the tuned LC-amplifier was connected to one of the deflection plates of the oscillograpn and the output of the untuned RC-amplifier to the other deflection plate. In this case the A.C. component in the bridge output is superposed on the action current of the fibre. In these arrangements, the condenser C, which had a capacity of the order of 10^{-10} farad, is short-circuited with a resistance of $2.5 \cdot 10^5$ ohms in the middle of the bridge; and consequently the presence of the condenser C brings about no appreciable deformation in the action current recorded.

It should be noticed in our records that the response of the LC-amplifier to an instantaneous alteration of bridge balance was relatively slow: it took about 0.5 msec or more to complete the response. Moreover, a great instantaneous variation in the potential difference between the electrodes, such as caused by a pronounced shock artefact, could result in a damping oscillation of a similar duration in the tuning circuit of the amplifier. But, since most of the experiments described in this paper were conducted at extremely low temperatures and the duration of the action current was correspondingly long, we could obtain reliable information concerning the time course of the impedance change accompanied by the production of the action current.

RESULTS

1. *The impedance of the resting nerve fibre and its variation during activity*

The fact that under these experimental conditions the resting impedance of the single nerve fibre is constantly well over 10 megohms has made all the high frequency

impedance measurements difficult. Frequencies over 10 kc were not used, because at such frequencies the capacity of the electrodes and the wires connected with them were considered to cause an appreciable error in the reading.

After the single fibre preparation was placed in the cooled nerve chamber and the temperature of the chamber became steady, the resting parallel resistance and capacity were measured at several frequencies between 2 and 6 kc. The resting resistance of the fibre, which could be obtained from the resistance of the known arms of the balanced bridge by multiplying the value of R in Fig. 1 by the ratio r_1/r_2, was in general between 20 and 60 megohms. It seemed fairly certain that this value varied according to the diameter and the internodal distance of the fibre. The value of Cr_2/r_1 in the balanced state was approximately 10^{-12} farad at a bridge frequency of 3 kc.

When the bridge was balanced with the LC-amplifier at a bridge frequency of about 3 kc, each sweep of the electron beam gave a narrow trace on the face of the oscillograph. A weak induction shock applied to the nerve fibre during the course of the sweep gave rise to a brief oscillation of the electron beam, due to the shock artefact. When the threshold was reached, the bridge went off balance and the oscillograph line was broadened into a band. Then, as the fibre recovered, the band soon narrowed down to the resting line again. In all cases the width of the band was found to vary directly as the strength of the bridge A.C. The balance was very stable and the measurement reproducible.

After the impedance change was recorded photographically as show in Fig. 2, top left, the oscillograph was switched from the LC-amplifier to the RC-amplifier (Fig. 1) and the action current of the fibre was recorded without change of the sweep circuit of the stimulus. As the bridge oscillator was not turned off in that case, the change in the impedance resulted in a slight broadening of the oscillograph line in the action current records obtained (Fig. 2, top right).

It is easy to demonstrate the impedance change during activity at the site of stimulation. With the experimental arrangements illustrated in Fig. 1, rectangular current pulses of varying strengths could be applied to the nerve fibre through the bridge electrodes. When the bridge was balanced with A.C., a rectangular current pulse applied to the same bridge electrodes brought about a deflection of rectangular configuration on the face of the oscillograph (connected to the RC-amplifier), due to overcompensation of the stimulating current by the bridge. After the rheobase was attained, action currents of all-or-none character and simultaneous changes in the impedance were observed (Fig. 2).

As the strength of the rectangular current pulse is increased, the time interval from the onset of stimulus to the start of action current decreases, and the form of the action current becomes correspondingly diphasic as a result of the increased internodal conduction time. At a strength sufficient to suspend conduction of impulse from one node of RANVIER to the other (between N_1 and N_2 in Fig. 1), the action current becomes completely monophasic. At this strength, the magnitude of the impedance change was found to fall to half the normal value.

More direct information on the magnitude of impedance change during activity can be obtained, according to the technique used by COLE AND CURTIS (1941) in their experiment on the squid giant axon, by the following procedure. The resistance and capacity of the known arm of the bridge, is so altered that the bridge is no longer balanced at rest, but it becomes balanced at some definite moment during the activity (see Fig. 3). In this way, the parallel resistance of the fibre (Rr_1/r_2) was shown to decrease by 5 to 15 % at the onset of the activity (at a bridge frequency of about 3 kc). Then, as the fibre recovers, the resistance returns to normal at a nearly constant rate until the band on the face of the oscillograph regains the resting width. The parallel capacity of the fibre (Cr_2/r_1) was found not to alter appreciably during activity.

The magnitude of the impedance loss during activity varies pronouncedly according

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to the bridge frequency. At higher frequencies the change was decidedly less. For frequencies above 7 kc it was not feasible to demonstrate any impedance change during activity.

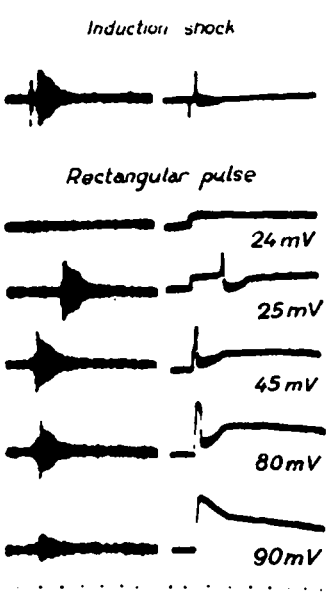

Fig. 2

Fig. 2. Left column: The impedance change during activity elicited by an induction shock (top) and rectangular current pulses (below). The bridge was balanced for the impedance of the nerve fibre at rest. The bridge frequency was 3 kc. The strength of the pulses are given in the figures. Right column: The bridge output amplified with untuned RC-amplifiers and recorded under otherwise the same condition as in the left column. The time marks at the bottom are 10 milliseconds apart. The temperature of the nerve chamber was 3.5° C.

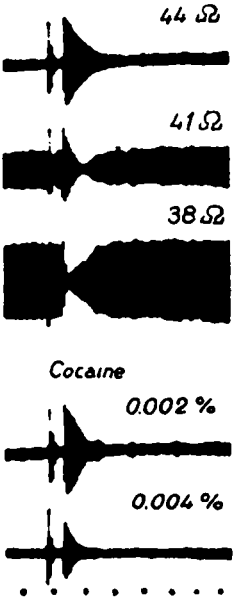

Fig. 3

Fig. 3. Bridge output during the passage of an impulse, with the bridge balanced at rest or at various moments during action. The numerals above indicate the parallel resistances in megohms of the fibre at the balanced moments. The two lower records were obtained after application of cocaine RINGER solutions of the concentrations indicated in the figures; the resting resistance of the fibre was increased by narcosis to about 48 megohms. Frequency 2 kc; temperature 5° C; time marks 10 msec apart.

2. The effects of alkaloids upon the time course of impedance change

Our previous investigation on the effect of alkaloids upon the isolated nerve fibre revealed that these drugs may be classified according to their physiological effects into three categories. Cocaine and many other alkaloids reduce the size and duration of the electric response of the fibre and raise the threshold; they may be referred to as narcotics. Sinomenine, brucine, emetine and heroine prolong the descending phase of the action current at adequate concentrations. Veratrine causes the fibre to produce a prolonged weak "after-current" which is the current counterpart of the negative after-potential. The classification of all alkaloids into these three types, namely into the cocaine-type, sinomenine-type and veratrine-type, become somewhat dubious at strong concentrations, as all chemicals are then narcotic in action.

In the present investigation, we have examined the effect of these three kinds of alkaloids upon the time course of the impedance change during activity. In the first place, the effect of cocaine, which is known to reduce the size and duration of the action current, was examined (Fig. 3). It was immediately disclosed that cocaine decreases the magnitude and duration of the impedance change during an action when applied to the region of the fibre around the impedance electrodes. At such strong concentrations as to inhibit completely the production of the action current, no impedance change was observed even at the site of stimulation.

We have investigated in the next place the effect of sinomenine. The drug was dissolved in RINGER at an adequate concentration (from 1 to 3%), and this solution replaced the fluid on both sides of the bridge-insulator. The fibre was excited from

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time to time by means of the induction coil. Alkaloids of this type are, unlike cocaine, progressive in action, *i.e.*, the magnitude of the effect increases gradually as time elapses even when the concentration of the drug remains unaltered.

It was demonstrated that this drug remarkably prolongs the period of decreased impedance. The magnitude of the impedance change on action is much less in the poisoned fibre than in the normal, but its effect upon the time course of the change is characteristic (Fig. 4). The course is such that the oscillograph line is broadened suddenly, then it soon narrows down to a certain extent and this level is maintained for some time until it finally begins to return gradually to normal.

The effect of veratrine upon the time course of impedance change during activity is very interesting in connection with its effect on the action current. It is possible to show the impedance counterpart of the increased negative after-potential, which a number of recent investigators have demonstrated for the nerve trunk (GRAHAM, 1930; GRAHAM AND GASSER, 1931; ACHESON AND ROSENBLUETH, 1941; KUFFLER, 1943 and others).

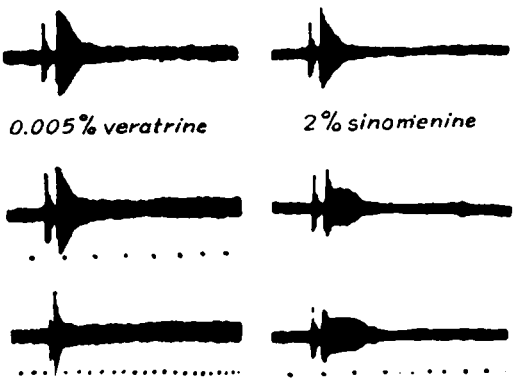

Fig. 4. Left column: The effect of veratrine as shown by photographic records of the impedance change during activity. The two lower records were obtained between 15 and 20 minutes after application of veratrine. The resting resistance was increased by the drug from 48 to 55 megohms. Frequency, 2 kc; temperature 5° C; time marks 10 msec apart. Right column: The effect of sinomenine. The two lower records were obtained about 5 and 15 minutes after application of the drug. The resting resistance was at first 50 megohms and was not much altered by the drug. Frequency 5 kc; temperature 6° C; time marks 10 msec apart.

When the RINGER's fluid on both sides of the bridge-insulator (Fig. 1) is replaced with a veratrine-RINGER solution of an appropriate concentration which varies considerably with the temperature, return of the impedance to normal following an action becomes incomplete and the band remains slightly broadened for a period of one minute or more after it has been once broadened. As the detection of the impedance change can be done fairly accurately even when the change occurs very slowly, it is obvious that, for the study of the process underlying the after-potential, the use of the impedance method is more adequate than the usual methods.

3. *The relationship between the impedance and the action current and the effect of polarization*

In order to examine the relationship between the magnitude of impedance change and the action current, a special technique was adopted, in which both the A.C. indicating the impedance changes and the action current were led simultaneoulsy into one and the same oscillograph. In the experimental arrangement shown in Fig. 1, these two components in the bridge output were amplified first by means of the RC-amplifier (1) and then the untuned RC-amplifier (2) made it possible to record action currents of the order of 10^{-9} ampere. The LC-amplifier, tuned to the bridge-A.C., had a current sensitivity of about 10 times as high as the RC-amplifier (2).

After a 0.2% cocaine-RINGER solution had been introduced into the distal pool of RINGER in which was immersed node of RANVIER N_2 in the figure, an induction shock

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applied to the fibre evoked an action current which was derived mainly from the activity at the node N_1. The time course of such an action current roughly duplicates that of the variation in the electromotive force at the plasma membrane of the node, namely the time course of the "action-e.m.f."

The action current records furnished in the left column of Fig. 5 were obtained with the arrangement of Fig. 1 in which the LC-amplifier was put out of action. Those in the middle column were obtained with the RC-amplifier (2) switched off. With all the amplifiers at work, the records in the right column were obtained.

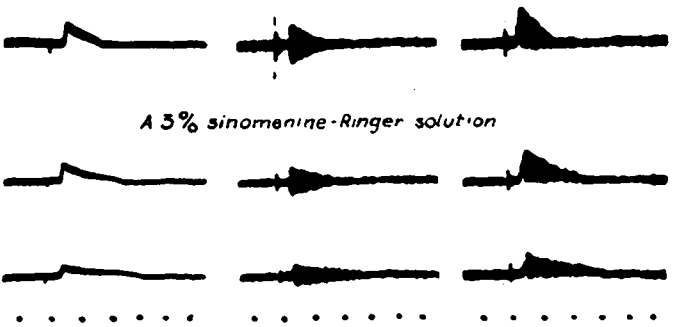

Fig. 5. Left column: "mononodal" action currents of a single nerve fibre. Middle column: Impedance changes during activity. Right column: Superposition of the impedance changes upon the action currents. Records in the two lower rows were obtained about 5 and 10 minutes after application of sinomenine respectively. Frequency 3 kc; temperature 3° C; time markers 10 msec apart.

When the sensitivity of the RC-amplifier (2) was reduced to such an extent that the maximum width of the band was approximately equal to the maximum deflection by the action current, superposition of these two components gave figures of which the lower margins showed practically no departure from the base line of the oscillograph. And this was true even after the node under observation (N_1) was poisoned with alkaloids (Fig. 5). This indicates undoubtedly that, if both the action current and the impedance change are limited to those derived mainly from the activity of a single node of RANVIER, *the magnitude of the impedance change is proportional to the strength of the action current at that moment.*

We came across an apparent exception to this rule in our investigation of the effect of polarization on the magnitude of impedance change during activity (Fig. 6). In this investigation, the battery circuit shown in Fig. 1 was used for the polarization of the fibre. The portion of the fibre in the distal pool

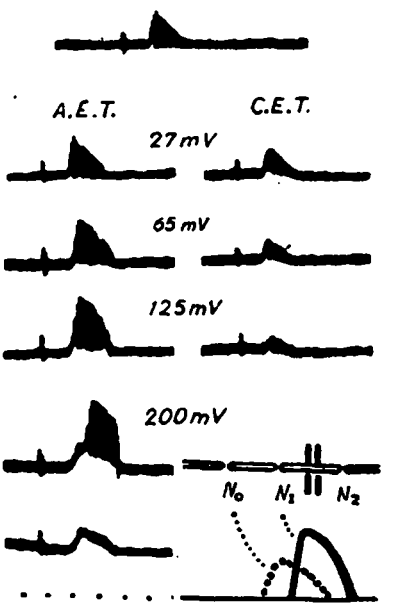

Fig. 6. Effect of electrotonic polarization upon the action current and the impedancec hange. Node N_2 in the figure was narcotized. The records in the left column were obtained during the anodal polarization of the node N_1 at various strengths, and those in the right column during cathodal polarization. Polarizing voltages are given in the figure. Two records at the bottom were taken at the same polarizing voltage. Frequency 2.8 kc, temperature 2.5° C, time marker 7 msec apart.

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was prevented from developing action currents by narcosis. The fibre was brought into action by an induction shock applied to its proximal portion after the polarizing current had been allowed to act for a period of about 0.5 second. In this experiment, the effect of the polarizing current is referred to as catelectrotonic (C.E.T.) when the node of RANVIER under observation (N_1 in Fig. 1) is on the side of the cathode of battery B in the polarizing circuit. When the sign of the battery is reversed, we speak of anelectrotonus (A.E.T.).

By C.E.T. these two types of electric responses are reduced in size, and by A.E.T. both are increased. In the case of C.E.T., the reduction in the magnitude of the impedance change was found to be more pronounced than that in the action current, but still a proportionality seemed to exist between these two types of response in that condition. In the case of very strong A.E.T., action currents without simultaneous change are often observed. A closer analysis of this phenomenon reveals, however, that this observed disparity between the action current and the impedance change is merely superficial.

As was first discovered by ERLANGER AND BLAIR (1934), the transmission of an impulse from one node to the next is strongly hampered by A.E.T. and consequently a notch is formed on the ascending limb of the action current record. In the diagram of Fig. 6, the broken line indicates the component of the action current derived from the node N_0 in the figure, and the thick continuous line shows the current from the node N_1. At the moment when the latter node N_1 is thrown into action, the oscillograph line changes over suddenly from the broken line to the continuous, producing a notch in the record (TAKEUCHI AND TASAKI, 1942).

With these points in mind, it is inferred that, under these experimental conditions, the component of the current arising from the activity of the node N_0 is unaccompanied by any observable change in the impedance. The observed impedance change is synchronous with and proportional to the deflection resulting from the action current of the node N_1.

DISCUSSION

One of the difficulties of our present investigation lies in the fact that, in order to demonstrate the change in the impedance during activity, only a restricted range of bridge frequency, 2–5 kc, is available. The limited duration of the action current determines the lower limit of the available frequency. The upper limit is influenced by the experimental fact that for higher frequencies no change in the impedance is observed during activity. This latter can no doubt be attributed to the properties of the myelin sheath which covers the nerve fibre.

There is evidence that the resistance of the myelin sheath is reactive in nature (TASAKI AND TAKEUCHI, 1942). For a direct current the sheath may behave like an almost perfect insulator, but, for a high frequency alternating current, it may act as though it were a good conductor. Adopting the view that the action current of the fibre arises from a process localized at the nodes of RANVIER, we may conclude that the inefficacy of a high frequency A.C. for detecting the impedance loss during activity is due to the leakage of the testing current through the myelin sheath.

In connection with our investigation of the effect of anodal polarization upon the impedance changes during activity, we have seen that the activity at the second node

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(N_0) from the bridge-insulator may cause a sizable action current in the bridge output without being accompanied by any detectable change in the impedance. We may now attribute this too to the above-stated property of the myelin sheath. The bridge A.C. cannot reach this remote node on account of leakage through the myelin sheath, while the action current from this node may spread to the bridge electrodes after suffering an appreciable distortion in its sharp rising phase.

Turning now to the relationship between the impedance change and the action-e.m.f. at the node of RANVIER, it should first be emphasized that these two occur not only simultaneously but also their magnitudes are proportional to each other at every moment during activity. The constant of proportionality may vary according to the experimental conditions, but during one specified activity, one varies proportionately to the other. This fact indicates undoubtedly that the change in the impedance and the production of the action current are two different expressions of one and the same bioelectric process which occurs at the plasma membrane. In the experiment of COLE AND CURTIS, the measurements were made under such conditions that the diphasic artefact and the spread of the action current along the fibre could cause a slight disparity between the time courses of these two processes.

In this connection, emphasis should be laid on the peculiarity of the time course of this bioelectric process. The first, rising phase is extremely short as compared with its second, descending phase. In this respect, the bioelectric responses we recorded are very like those obtained with the plant cell Nitella (see for example OSTERHOUT AND HILL, 1936, p. 46).

It would be very interesting to know how this bioelectric process is affected by various chemical and physical agents such as those used in the present investigation. It is first necessary to show that the changes in the bioelectric response described above are the real effects of those agents. Their effects upon the resistance of the myelin sheath must be excluded before we can discuss the process at the node.

By the shock test method in combination with a bridge-insulator (TASAKI, 1940), it has been demonstrated that, by cocaine of above 0.2% and urethane of above 2%, the resistance of the myelin sheath is increased beyond the limit of the experimental error. In the present investigation, introduction of a 2% cocaine solution into one of the pools on the bridge-insulator increased the parallel resistance by about 5%.

With a view to clarifying the effect of the polarizing current upon the resting resistance of the nerve fibre, we have made a special experiment in which a three-electrode arrangement with the bridge-insulator technique was used. Of the three electrodes two served as the bridge-electrodes for the impedance measurement, and the remaining one in combination with one of the bridge-electrodes was used for polarizing the fibre. In the middle pool of RINGER in which the common electrode was immersed, a short portion of the fibre was introduced including one node of RANVIER. In this manner it has been shown that A.E.T. of about 100 millivolts brings about no detectable change in the resting impedance and that a slight, but unmistakable change results in case of C.E.T. of about 100 millivolts. This catelectrotonic effect is considered indistinguishable from the impedance counterpart of the after-potential which is known to increase in case of C.E.T. (GRAHAM, 1942).

Thus, all the effects of the chemical and physical agents under investigation upon the resting impedance are too small to account for the observed impedance change during activity. We may therefore conclude that all the remarkable effects brought

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about by alkaloids and polarization are due to their direct action upon the action current producing process at the plasma membrane.

Among the data presented, the fact that A.E.T. augments the magnitude of the impedance changes during activity may be of considerable interest in regard to the mechanism of action current production. This seems to indicate that, contrary to the conclusion at which COLE AND CURTIS have arrived for the squid giant axon, the decrease in the membrane resistance during activity is not so profound as to be regarded as a complete depolarization of the membrane. If the resistance of the normal plasma membrane is decreased on action by almost 100% it would be impossible for the impedance during activity to by augmented by any kind of agent which brought about no change in the resting resistance.

Some of our previous results, however, strongly suggest that the ohmic resistance of an active plasma membrane would be practically zero compared with its resting resistance (TASAKI, 1940; TASAKI AND TAKEUCHI, 1942). Neither stimulating nor action current spreads beyond an active node of RANVIER. But, since the accuracy of this method of measuring the membrane resistance falls far below the direct impedance measurement, it would probably be possible to find a way to reconcile these two sets of experimental results without introducing any complicated assumptions.

We wish to express to Dr WASABAYASHI AND Dr KATSUKI our appreciation of their kindness in lending us some experimental equipment; and to Dr OCHIAI AND Dr MIYAGI our thanks for supplying us with alkaloids.

SUMMARY

1. High frequency alternating current impedance measurements have been made, during rest and activity, on isolated single nerve fibres of the toad.

2. During activity there is a decrease in the impedance of the plasma membrane at the nodes of RANVIER. The time course of the impedance loss is the same as that of the "action electromotive force" set up at the plasma membrane.

3. The impedance change and the action current production are two different expressions of one and the same bioelectric process which occurs at the plasma membrane.

4. Cocaine and many other alkaloids reduce the magnitude and duration of the bioelectric response. Sinomenine and several other alkaloids prolong the duration of the response in a very characteristic manner. Veratrine retards complete recovery from a previous activity.

5. Catelectrotonus depresses and anelectrotonus enhances the bioelectric process.

RÉSUMÉ

1. Des mesures d'impédance ont été faites sur des fibres nerveuses isolées, de crapaud, au cours du repos et de l'activité, à l'aide de courant de haute fréquence.

2. Au cours de l'activité, il y a une diminution de l'impédance de la membrane protoplasmique aux noeuds de RANVIER. La diminution de l'impédance en fonction du temps est la même que celle de la "force d'action électromotrice" qui se manifeste à la membrane protoplasmique.

3. Le changement d'impédance et la production du courant d'action représentent deux manifestations différentes d'un seul et même phénomène bioélectrique qui a lieu à la membrane protoplasmique.

4. La cocaïne et de nombreux autres alcaloïdes réduisent la grandeur et la durée de la réponse bioélectrique. La sinoménine et plusieurs autres alcaloïdes prolongent la durée de la réponse d'une façon très caractéristique. La veratrine ralentit le retour à la normale après activité.

5. Le catélectrotonus diminue et l'anélectrotonus augmente le phénomène bioélectrique.

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ZUSAMMENFASSUNG

1. Die Impedanz von Hechfrequenz-Wechselströmen sowohl im Ruhe- als im Arbeitszustand, wurde an isolierten Nervensträngen der Kröte gemessen.

2. Während der Arbeit findet eine Abnahme der Impedanz der Plasma-Membran bei den RANVIER-Knoten statt. Der Zeitverlauf dieses Impedanz-Verlustes ist der Gleiche als der der "elektromotorischen Wirkungskraft" welche an der Plasma-Membran entsteht.

3. Die Impedanz-Änderung und die Erzeugung des Wirkungsstromes sind zwei verschiedene Ausdrücke eines und desselben bioelektrischen Prozesses, welcher an der Plasma-Membran stattfindet.

4. Cocain und viele andere Alkaloide verringern die Grösse und Dauer der bioelektrischen Ansprechung. Sinomenin und verschiedene weitere Alkaloide verlängern die Dauer der Ansprechung in sehr charakteristischer Weise. Veratrin verzögert die völlige Erholung von vorgängiger Arbeit.

5. Katelektrotonus senkt und Anelektrotonus erhöht den bioelektrischen Prozess.

REFERENCES

G. H. ACHESON AND R. ROSENBLUETH, *Am. J. Physiol.*, 133 (1941) 735–751.
K. S. COLE AND H. J. CURTIS, *J. Gen. Physiol.*, 22 (1939) 37–64.
K. S. COLE AND H. J. CURTIS, *J. Gen. Physiol.*, 22 (1939) 649–670.
K. T. GRAHAM, *J. Pharmacol. Exptl Therap.*, 39 (1930) 268–269.
K. T. GRAHAM AND H. S. GASSER, *J. Pharmacol. Exptl Therap.*, 43 (1931) 163–185.
J. ERLANGER AND E. A. BLAIR, *Am. J. Physiol.*, 110 (1934–35) 287–311.
S. W. KUFFLER, *J. Neurophysiol.*, 8 (1943) 113–120.
H. LULLIES, *Pflügers Arch. ges. Physiol.*, 225 (1930) 87–97.
A. ROSENBLUETH, J. REBOUL, AND A. M. GRASS, *Am. J. Physiol.*, 130 (1940) 527–538.
W. J. V. OSTERHOUT AND S. E. HILL, *Cold Spring Harbor Symposia Quant. Biol.*, 4 (1936) 43–52.
I. TASAKI, *Pflügers Arch. ges. Physiol.*, 244 (1940) 125–141.
I. TASAKI AND T. TAKEUCHI, *Pflügers Arch. ges. Physiol.*, 245 (1942) 464–482.
T. TAKEUCHI AND I. TASAKI, *Pflügers Arch. ges. Physiol.*, 246 (1942) 33–43.

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