EFFECT OF THE ANODE AND CATHODE OF A DIRECT CURRENT ON THE ELECTRICAL ACTIVITY OF THE ISOLATED NODE OF RANVIER IN A MEDIUM WITH LOW SODIUM CONCENTRATION AND DURING THE ACTION OF NOVOCAIN

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Previous investigations have shown that the action of Novocain on the isolated node of Ranview lowers the amplitude of the action potential (AP). With high concentrations of Novocain the AP disappears completely [1]. Similar changes in the electrical activity in the node may be obtained with a lowering of the concentration of Na ions in the external solution [5, 8, 15, 16]. This similarity may be understood in terms of the sodium theory of genesis of the AP, following the ideas of Shanes that Novocain and other local anesthetics cause marked depression of the permeability of the membrane to Na ions during excitation [10, 14].

From another point of view the similarity between the changes in the AP in a medium with a low sodium concentration and during the action of anesthetics may be attributed to he fact that, in a medium with low sodium concentration certain chemical substances depressing the AP are secreted in the membrane of the node of Ranview [13]. If this latter hypothesis is correct, it would be expected that the depression of the AP caused by removal of Na ions from the solution may be abolished by the anode of a direct current just as is observed in the case of depression by Novocain [9].

The present investigation, carried out under the direction of B. I. Khodorov, was aimed at verifying this hypothesis by comparing the action of the dc anode and cathode on the node of Ranvier in a medium containing a low sodium concentration and during the action of Novocain.

EXPERIMENTAL METHOD

The test object consisted of isolated fibers of the sciatic nerve of the frog (Rana temporaria). The nerve fiber was dissected by a slight modification of the Kato-Tasaki method [11, 12]. Stimulation, polarization, and recording of the electrical activity from a single node of Ranvier were carried out by means of a three-electrode device described in previous communications [2, 4]. The isotonicity of the solutions with a low sodium concentration was maintained by saccharose. The experiments were performed at 19-22°.

EXPERIMENTAL RESULTS

With a decrease in the concentration of Na ions ([Na]) in the Ringer's solution the amplitude of the AP of the isolated node of Ranvier diminished (Fig. 1A). A sharp fall in the amplitude of the AP took place when the [Na] concentration fell below 20%. In solutions with a [Na] concentration below 5% the AP disappeared, and only local responses could be recorded in the node, their magnitude varying with the strength of the stimulus. Replacement of the solution with low sodium concentration by normal Ringer's solution completely restored the amplitude of the AP to

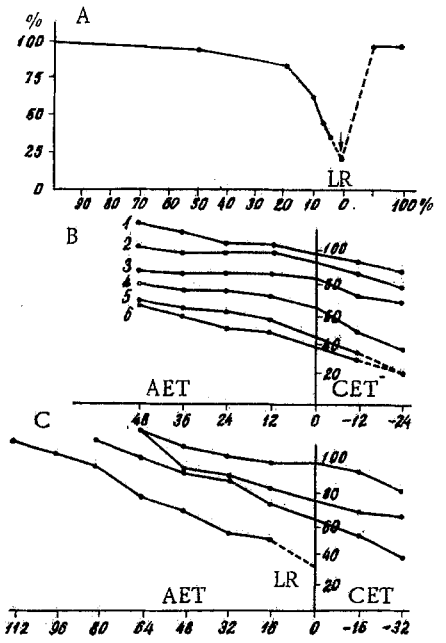

Fig. 1. A—relationship between amplitude of AP and concentration of Na ions in solution. Axis of ordinates—amplitude of AP (as % of initial); axis of abscissas—concentration of sodium ions in solution (in %, concentration of Na ions in Ringer's solution taken at 100%). The arrow indicates replacement of medium with low Na concentration by Ringer's solution; LR—local response; B—relationship between amplitude of AP of node of Ranvier and strength of polarizing current: 1—in Ringer's solution; 2, 3, 4, 5, 6—in solutions with ion concentrations of 50, 20, 10, 8, and 5% respectively. Axis of ordinates—amplitude of AP (in %, amplitude in Ringer's solution taken as 100%); axis of abscissas—voltage of polarizing current (in mV); AET—anelectrotonus; CET—catelectrotonus; C——relationship between amplitude of AP of node of Ranvier and strength of polarizing current: 1—in Ringer's solution; 2,3,4,——during action of Novocain in concentrations of 10^{-5}, 5×10^{-5}, and 10^{-4} respectively.

its initial value. Polarization of the node of Ranvier in Ringer's solution by a direct current modified the amplitude of the AP. The relationship between these changes and the strength of the acting direct current is shown in Fig. 1B, curve 1. The anode of a direct current with a strength equal to twice the rheobase increased the amplitude of the AP by 20%, and the cathode lowered it by approximately the same amount when the strength of the polarizing current was equal to 1 rheobase.

The action of a direct current on a node, the electrical activity of which was depressed by a solution with a low sodium concentration, led to the same changes in the amplitude of the AP as in Ringer's solution, i.e., to an increase under the anode and a decrease under the cathode. The nearly parallel curves 2-6 in Fig. 1 B reflect these changes in the AP: during the action of the cathode on the node kept in a solution with a [Na] concentration of 5-8% the AP disappeared and was replaced by a local response. Attention was drawn to the fact that the increase in the amplitude of the AP under the anode in the medium with low [Na] concentration was approximately the same as in Ringer's solution. This is clearly seen in Fig. 2, where two responses before and after the action of the anode on the node of Ranvier are superimposed in each frame.

Curves reflecting the relationship between the amplitude of the AP of the novocainized node and the strength of dc polarization are given in Fig. 1C. Under the anode the amplitude of the AP, lowered by Novocain, was restored. Under the cathode marked depression of the AP took place, as in the medium with a low [Na] concentration. While the amplitude of the AP in a medium with a low [Na] concentration or during the action of Novocain fell, the critical level of depolarization of the membrane (Fig. 3A) rose. In a solution with a 5% [Na] concentration and with a 10^{-4} concentration of Novocain the critical level rose to 200% and higher. The action of the direct current modified the magnitude of the critical level almost equally in the medium with a low [Na] concentration and in the solution of Novocain (Fig. 3A and B). In both cases the anode depressed the critical level while the cathode, on the other hand, increased it sharply. However, the critical level, when lowered under the anode, still remained much higher than the initial value.

The change in the amplitude of the AP in the isolated node of Ranvier caused by a lowering of the [Na] concentration and that caused by Novocain are externally similar. However, a dc anode, when applied to the node, very slightly increased the response depressed by the solution with the low [Na] solution but almost completely restored the amplitude of the AP of the node depressed by Novocain. This difference in the effects of the anode conflicts with Tasaki's views regarding the common mechanism of action of solutions with a low [Na] concentration and of anesthetics on the membrane of the node [13]. On the other hand, these results may be satisfactorily explained by the theory of Hodgkin and Huxley [7], according to which the decrease in the AP and the increase in the thresholds of depolarization in a medium with a low sodium concentration take place as a result of a lowering of the equilibrium potential for Na ions and, consequently, of a weakening of the inflowing sodium stream [8]. The dc anode does not alter the permeability of the membrane to Na ions, and therefore, cannot restore the AP in a medium with low [Na] concentration. The small increase in amplitude under the anode both in Ringer's solution and in a medium with a low [Na] concentration is the result of removal of depolarization of the membrane, which always occurs in the isolated nerve fiber [6]. A decrease in the intensity of the inflowing sodium stream also takes place when

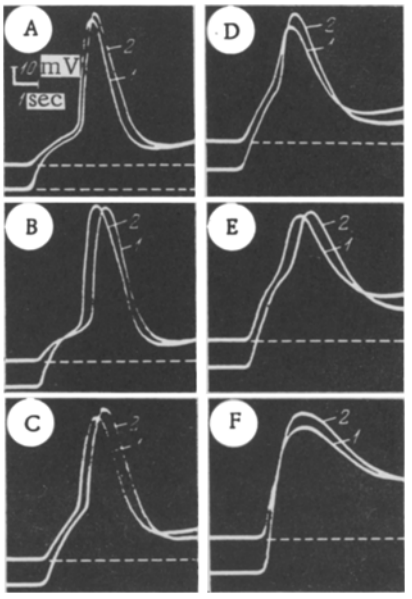

Fig. 2. Effect of anode of a direct current on AP of an isolated node of Ranvier. A—in Ringer's solution; B—in solution with Na ion concentration of 50%; C—20%; D—8%; E—5%; F—1%; 1—before polarization with anode; 2—during polarization.

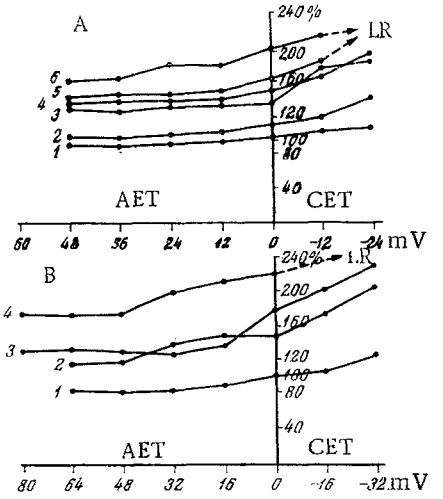

Fig. 3. A—relationship between critical level of depolarization (LD) of a node of Ranvier and strength of polarizing current. 1—in Ringer's solution; 2,3,4,5,6—in solution with Na ion concentration of 50, 20, 10, 8, and 5% respectively; B—relationship between critical level of depolarization of node of Ranvier and strength of polarizing current; 1—during action of Novocain in concentrations of 10^{-5}, 5×10^{-5}, and 10^{-4} respectively. Axis of ordinates—critical level (in %, critical level in Ringer's solution taken as 100%); axis of abscissas—voltage of polarizing current (in mV). Remainder of legend as in Fig. 1.

Novocain acts on the isolated node of Ranvier, but it is due, not to a lowering of the equilibrium sodium potential, but evidently to an increase in the degree of inactivation of the sodium conductivity of the membrane. In this case the dc anode, when applied to the novocainized node, weakens or completely removes the inactivation of the membrane, as a result of which the amplitude of the AP is restored. This explains why in our experiments the amplitude of the AP increased very slightly under the anode in the solution with a low [Na] concentration, whereas in the node depressed by Novocain it was almost completely restored.

The dc cathode, when applied to the node, depolarizes the membrane and intensifies its inactivation. As a result of this process the AP is lowered under the cathode both in the medium with a low [Na] concentration and during the action of Novocain.

As a result of the fall in the intensity of the inflowing current in the medium with a low [Na] concentration and in the Novocain solution the critical level of depolarization, as might be expected, rose [10]. The effect of the cathode increased it still further while the anode, on the contrary, slightly depressed it. However, complete restoration of the critical level to its normal value did not occur under the anode either in the medium with low [Na] concentration or in the Novocain solution. At the same time the amplitude of the AP of the novocainized node, as mentioned above, was fully restored under the anode. This disparity between the changes in the critical level and AP during the action of an anode current on a node depressed by Novocain is difficult to explain in accordance with the theory of Hodgkins and Huxley. The problem of the nature of the processes determining the thresholds of depolarization of the membrane is extremely complex and requires special study [3].

SUMMARY

Experiments were performed on single nerve fibers of Rana temporaria. The changes in the value and the form

of action potential (AP) proved to be similar both in a low-sodium medium and in a Novocain solution. The action of a dc anode on the node of Ranvier in a low-sodium medium caused only an insignificant rise of the AP amplitude but restored the AP completely in a node treated with Novocain. The cathode placed on the node stressed the AP in both cases. The membrane depolarization critical level (CL) rose both in a low-sodium medium and in a Novocain solution. Direct current cathode raised CL to a still greater degree, whereas the anode, on the contrary, lowered it somewhat. However, complete CL restoration did not occur either in a low-sodium medium or in a Novocain solution. The possible mechanism of the changes occurring in the AP and CL amplitudes during dc polarization in a low-sodium medium and in a Novocain is discussed.

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