MODIFICATION OF THE ELECTRIC RESPONSE OF A SINGLE RANVIER NODE BY NARCOSIS, REFRACTORINESS AND POLARIZATION

ICHIJI TASAKI, KANJI MIZUGUCHI, AND KYOJI TASAKI
Physiological Institute, Keio University, Yotsuya, Tokyo and Tokugawa Biological Institute, Mejiro, Toshima-ku, Tokyo

(Received for publication January 29, 1948)

THE PRESENT investigation is undertaken to show how the physiological properties of the plasma membrane at the node of Ranvier is modified by narcosis, the relatively refractory period and electrotonus. We have already dealt with this problem in previous papers (5, 6), and the present study confirms and expands the previous results.

METHODS

Toad's rapid motor nerve fibers, singled out of sciatic-gastrocnemius preparations, were used for the experiments exclusively. The fiber was mounted across two sets of bridge-insulator. Action currents from a single Ranvier node were recorded by the use of a tripolar arrangement (Fig. 1, left top). In each one of the three independent pools of Ringer (shaded area in Fig. 1) a Zn-$ZnSO_4$-Ringer electrode was immersed. The electrode in the middle was common to the exciting circuit and to the current-recording circuit. One (right in Fig. 1) was led to the grid of the amplifier. The grid-lead was connected with the ground-lead (in the middle) with resistances (R and R′) of about 10^5 ohms. Two stimulating circuits, one for rectangular current pulses and the other for induction shocks (or at times for polarizing currents), were connected in series, and one of the terminals was led to the remaining electrode (on the left). The portions of the nerve fiber in the two lateral pools were deprived of their excitability by replacing the fluid in them with a 0.3 per cent cocaine-Ringer solution.

RESULTS

Rheobase and action current during refractory period. A long rectangular current pulse applied to a Ranvier node during the relatively refractory phase produces a nerve impulse, if it is effective at all, within 2 or 3 msec. after the onset of the pulse (at about 20°C.). It was therefore possible to determine at any moment during the refractory period the critical strength of such pulses required to excite the node. The height of the spike thus evoked was naturally smaller than that of a normal one elicited after the end of the refractory period.

In the present study, the first conditioning stimulus was an induction shock of strength double the threshold. In Figure 1A, right, the uppermost record shows the action current of a single Ranvier node elicited by an induction shock of threshold strength. The second record shows the responses of a resting node to a rectangular current pulse of 10 msec. in duration. Other records in the figure were obtained by applying long current pulses of threshold strengths at various moments during the refractory period left behind by the first impulse.

Action currents were generally found to be released in all-or-none manner even during the refractory period. But, when the interval between the first shock and the onset of the rectangular pulse became critically short, *i.e.*, when the second stimulus falls at a moment immediately after the absolutely refractory period, spikes with variable size and form were observed with current pulses of threshold strength. Especially when the node was under

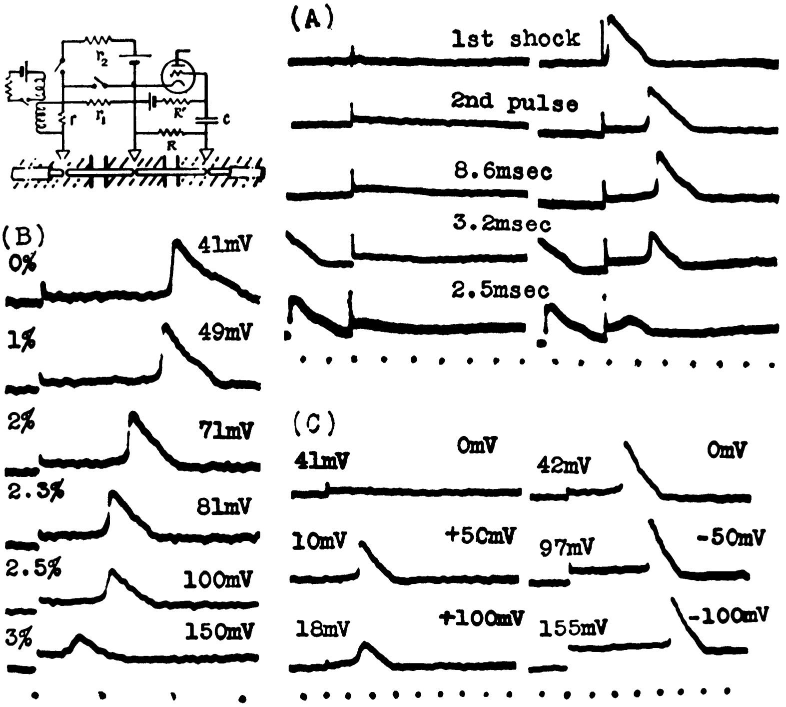

FIG. 1. Action currents of a single Ranvier node under various experimental conditions. Diagram in the corner shows the arrangements used for obtaining the records of (A); $r = 5k\omega$, $r_1 + r_2 = 1$ $k\omega$, $R = 100$ $k\omega$ and $R' = 500$ $k\omega$. (A): Action currents of a node in the refractory period. Uppermost pair of records shows the response of the node to the first, induction shock of just below (left) and above (right) threshold strength. Second pair gives the response to the second pulse alone; strength of the pulses, 46 mV. (left) and 48 mV. (right). In the remaining records, the intervals between the first shock and the make of the second pulse are given. Strengths of the pulses: in the 3rd pair 50 and 52 mV., in the 4th 66 and 68 mV., in the 5th 92 and 95 mV. In the last two pairs the first conditioning responses are seen. 20°C. (B): Action currents of a narcotized node. Concentration of urethane and voltage used (all rheobasic) are given in the records. 24°C. (C): Action currents of a node under electrotonus. The polarizing (right) and the stimulating voltages (left) are written in the records. 20°C. Time, 1 msec. For the absolute strengths of action currents recorded, see corresponding diagrams in Fig. 2.

weak narcosis, the variability in the spike-form was conspicuous. Even in such a case, however, current pulses above 110–120 per cent the threshold strength induced spikes of fairly constant configuration. The solid lines in Figure 2A give the relationship between the spike-height or the threshold (as ordinate) and the time interval from the first shock to the spike (as abscissa). As the testing current pulses had a long duration, it may be absurd to speak of the threshold value at a definite moment. Taking the interval between the first shock and the second spike as abscissa in this figure is merely tentative. The broken lines in Figure 2 present a similar result obtained after application of a dilute narcotic (a 2 per cent urethane) to the Ranvier node under consideration. It will be seen in this figure that the recovery of the spike height and threshold to the resting level takes place earlier in a narcotized node than in a normal.

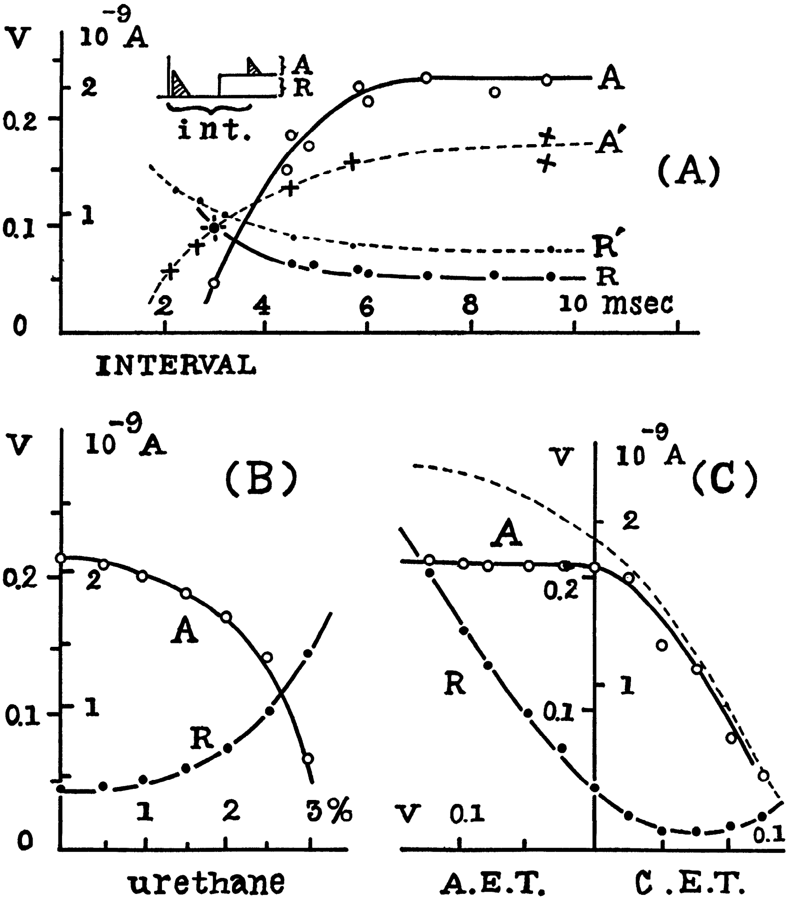

FIG. 2. Rheobase and spike height of a single node during the refractory period (A), under urethane narcosis (B) and under electrotonus (C). Some of the records from which these diagrams are constructed are presented in Figure 1.

Narcosis. When a narcotizing solution is introduced into the middle pool in which the single node under investigation is immersed, the threshold is raised and the spike height is reduced immediately to the level which depends upon the concentration of the narcotic employed. Records in Figure 1B were obtained when long rectangular current pulses of threshold strengths were applied to such a narcotized node. The concentration of the narcotic—urethane in this case—was increased step by step until finally the spike height was reduced so that it became difficult to make accurate measurements. It will be noticed in these records that the latent period for a current pulse of the rheobasic strength is shortened with increasing concentration of narcotic, while the crest time of the action current is distinctly lengthened by narcosis.

Two curves in Figure 2B (experiment of Fig. 1B) shows how the rheobase and the spike height of a single Ranvier node changes with increasing concentration of the narcotizing solution in which the node is immersed. In this experiment, a 3 per cent urethane-Ringer solution was not sufficient to remove the excitability of the node completely; but, in most of the previous experiments, we have seen that about 2.5 per cent was sufficient.

In all these diagrams, just as in those in previous articles (6), the two curves are drawn in such a manner that the normal spike height is about five times as high as the normal rheobase. This is to facilitate our consideration of transmission along an impaired region of a nerve fiber. For the details of such a discussion, one may refer to the previous articles.

Polarization. To apply a polarizing current to a single Ranvier node, a polarizing circuit was connected in series with the stimulating circuit, instead of the induction coil shown in the diagram of Figure 1. The polarizing circuit consisted, just as did the stimulating circuit, of a battery, two resistances and two knock-over keys of the Helmholtz pendulum. In the present study, the knock-over keys of the pendulum were so set that the polarizing current started 11 msec. before the onset of the long rectangular current pulse by which the spike to be recorded was evoked.

In the preliminary experiments it has been shown that the electrotonic changes in the spike height and threshold described here take place within about 10 msec. from the onset of the polarizing current and this state is then maintained steadily for about 100 msec. thereafter. Recovery from the catelectrotonus (C.E.T.) occurs in about 5 msec. after withdrawal of the polarizing current, provided that the duration of the polarizing current does not exceed about 100 msec.

Diagram C in Figure 2 (experiment of Fig. 1C) shows that C.E.T. reduces both the spike height and the rheobase and that anelectrotonus (A.E.T.) increases both. Change in the spike height by C.E.T. is remarkable, but that brought about by A.E.T. is slight, especially when long rectangular current pulses of rheobasic strengths are employed to induce the action currents. When, however, brief current pulses were used for the test, it was observed that the spike height can be increased considerably by A.E.T. and can reach about 130 per cent the normal height in favorable cases. The dotted line in Figure 2C shows the result obtained when pulses of 0.6 msec. were used as testing shocks in the same preparation. The fact that long testing current pulses diminish the anelectrotonic change in the spike height indicates that such testing current pulses, which are of the opposite sign and are always stronger than the polarizing pulse, counteract the anelectrotonic effect before they can produce action currents. In other words, a testing current can bring about a catelectrotonic effect in itself, if it is allowed to act upon the node for several milliseconds.

It will also be seen in Figure 2 that the rise of the rheobase by A.E.T. is approximately proportional to the polarizing voltage used. This means that, if we regard the polarizing current as a part of the stimulating current, there is only a slight change in the threshold in the case of A.E.T.; that is to say, excitation occurs when the algebraic sum of the polarizing and testing currents rises above the normal rheobase. To be more exact, however, the sum of the polarizing and testing voltages is always greater than the normal rheobasic voltage in A.E.T. as well as in C.E.T.

Another feature which has been brought to light by the present investition is the change in the form of the action current by electrotonus. It will be clearly seen in the records of Figure 1C that the crest time of the action current is lengthened by C.E.T. and shortened by A.E.T., although in the latter case this time is too short to be determined accurately. It is interesting in this connection that the latent period—following which the action current is released after the make of the testing current pulse of rheobasic strength—is influenced by electrotonus in a reversed manner as the crest-time, *i.e.*, it is shortened by C.E.T. and lengthened by A.E.T.

In the experiments in which the action of a fiber or a group of fibers lying in the nerve trunk was taken as index, results considerably different from that of Figure 1C seem to be obtained. Chweitzer's data (1, 2), for example, show the presence of another inflection in the rheobase-electrotonus curve on the side of A.E.T., corresponding to the break-excitation at anode. Data of Erlanger and Blair (3), to cite another example, indicate a remarkable increase of the spike height in A.E.T. It seems to us that all these discrepancies in the experimental results can be accounted for as due to the complex character of the electrical net-work in the nerve trunk, especially to the highly polarizable character of the myelin sheath of the fiber in question or of the neighboring fibers.

SUMMARY

By the method of bridge-insulator, records were taken of the action currents arising from a single Ranvier node of a toad's nerve fiber. It has been shown that narcosis, refractoriness and electrotonus bring about such modifications in the rheobase and electric response as shown in the figures.

REFERENCES

1. CHWEITZER, A. Recherches sur les lois de la stimulation électrique des nerfs, envisagée comme une variation d'intensité de sens constant. *Arch. int. Physiol.*, 1935, *40:* 398–421.
2. CHWEITZER, A. Recherches sur les diverses modalités de l'excitation électrique des nerfs par variation brusque. *Ann. Physiol. Physicochim. biol.*, 1937, *13:* 239–293.
3. ERLANGER, J. and BLAIR, E. A. Manifestations of segmentation in myelinated axons. *Amer. J. Physiol.*, 1934–1935, *110:* 287–311.

4. TAKEUCHI, T. and TASAKI, I. Uebertragung des Nervenimpulses in der polarisierten Nervenfaser. *Pflüg. Arch. ges. Physiol.*, 1942, *246:* 33–43.
5. TASAKI, I. and TAKEUCHI, T. Der am Ranvierschen Knoten entstehende Aktionsstrom und seine Bedeutung für die Erregungsleitung. *Pflüg. Arch. ges. Physiol.*, 1941, *244:* 696–711.
6. TASAKI, I. and TAKEUCHI, T. Weitere Studien über den Aktionsstrom der markhaltigen Nervenfaser und über die elektrosaltatorische Uebertragung des Nervenimpulses. *Pflüg. Arch. ges. Physiol.*, 1942, *245:* 764–782.