# ROLE OF AFTER-DEPOLARIZATION IN FIBER INTERACTION WITHIN THE NERVE TRUNK

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In response to electrical stimulation of a frog sciatic nerve preparation at 30-50/sec, a gradual increase in amplitude of the action potentials is observed. This increase is based on an after-increase in the excitability of the nerve fibers.

Electrical changes developing in a nerve trunk during the passage of impulses along individual fibers can exert a substantial influence on the functional state of neighboring, nonfunctioning fibers. This is manifested by changes in their excitability and, under certain conditions, by the onset of spreading excitation [3, 4, 8, 9]. A mathematical analysis of this interaction for nonmedullated fibers has recently been given by Markin [5]. However, in the investigations cited, attention was concentrated on interaction between fibers actually during the generation of the spreading spike. However, reports have been published [10, 11] that in some cases the change in the properties of nonfunctioning fibers can also be exhibited for tens or even hundreds of milliseconds after the spike.

The object of the present investigation was to analyze some of the conditions under which this prolonged interaction between fibers is found, and to establish the connection between this phenomenon and the phase of after-depolarization of the membrane.

## EXPERIMENTAL METHOD

Altogether 150 experiments were carried out on the isolated sciatic nerve of the frog Rana temporaria. The proximal end of the nerve was stimulated by single, paired, or regular square pulses from an electronic stimulator with radiofrequency output. Action potentials were recorded from the distal end of the nerve, in some experiments by silver electrodes, and in others with nonpolarizing Ag– AgCl electrodes (interelectrode distance 2.5-3 cm). When monopolar recording was used, the segment of the nerve beneath the distal electrode was killed by crushing it with forceps or by the application of hot physiological saline. Action potentials were amplified and recorded by means of a 5-channel UFUPT-5 instrument (made at the experimental workshops of the Institute of Experimental Medicine, Academy of Medical Sciences of the USSR).

## EXPERIMENTAL RESULTS

Under ordinary conditions, responses of a freshly prepared specimen of the nerve from autumn frogs to comparatively infrequent, regular stimulation remained unchanged throughout the period of stimulation. With an increase or decrease in the strength of the stimuli, the amplitude of both the first and the subsequent responses in a regular series increased or decreased correspondingly; only if the frequency of stimulation was higher than 150-300/sec was the nerve response depressed: the action potentials progressively diminished during stimulation. No increase in amplitude of the responses ever took place during regular stimulation of these preparations.

However, under certain conditions a completely different picture was observed. In response to stimuli of submaximal strength, the action potentials of the nerve during repetitive stimulation gradually began

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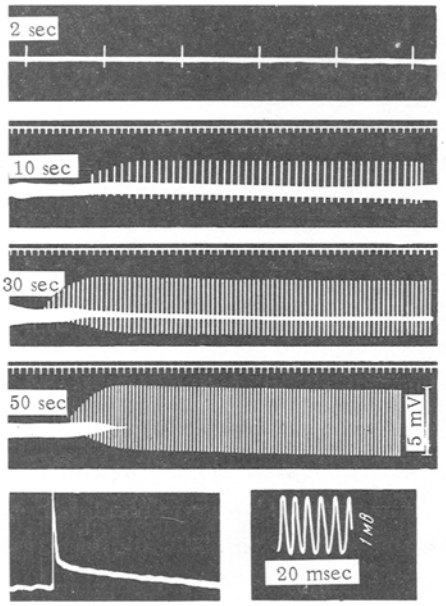


Fig. 1

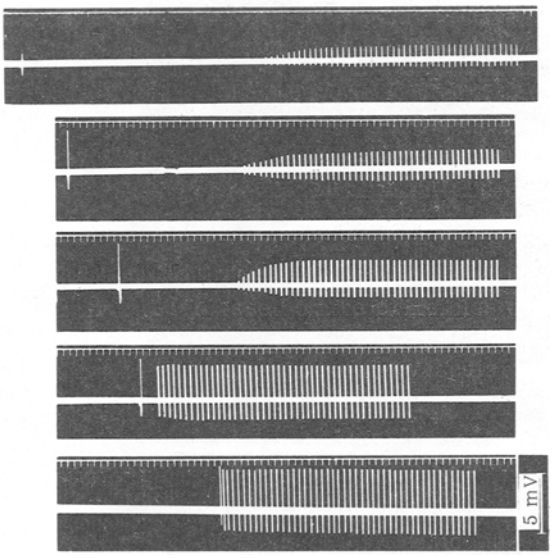


Fig. 2

Fig. 1. Increase in amplitude of action potentials of nerve after changes produced by gentle drying in air. Time marker 50 msec. Single action potential with monopolar recording and calibration signal for it (interval between peaks 20 msec).

Fig. 2. Changes in amplitude of testing action potentials of altered nerve (air-dried) depending on duration of interval after conditioning stimulus. Time marker 50 msec.

to increase and could ultimately be several times greater in amplitude than the response to the first stimulus. The rate and degree of increase of the nerve response under these conditions varied depending on several factors, the most important of which was the initial functional state of the preparation. If the nerve was first kept in Ringer's solution, then dried gently and kept for a short time in hypertonic solution with an increased NaCl concentration, the rate and degree of this phenomenon were increased.

Other conditions being equal, the degree of the increase in amplitude of the action potentials was largely dependent on the frequency of stimuli applied: within certain limits, the higher the frequency the sharper and greater the increase in amplitude of the action potentials. The records (Fig. 1) show that a slight increase in amplitude of the action potentials occurred at a frequency of 2/sec. The optimal frequency of stimulation, at which this increase was most clearly exhibited, was 30-50/sec. It is interesting to note that at optimal frequencies of stimulation the increased amplitude of the action potentials was highly stable and could persist for 5 min or more without any marked sign of a decrease. This suggests that at optimal frequencies of stimulation, a high level of excitability is maintained throughout, and each impulse evidently leaves behind it a trace, in the form of increased excitability. In fact, if after stimulating the nerve at subthreshold strength and at the optimal frequency for exhibition of summation (30-50/sec), the strength of stimulation was increased up to the threshold or above it, and then again, without stopping the stimulation, it was steadily weakened down to subthreshold values, the nerve continued to respond, thereby exhibiting a unique form of facilitation.

To obtain the final solution to the problem of whether, in these cases, there is an after-increase of excitability, a special series of experiments was carried out to measure the threshold of excitability both after a single stimulus and after a series of stimuli, i.e., during repetitive activity of the nerve. Under these conditions the strength of the testing stimulus was at the threshold level, and the duration of the phase of exaltation was judged from the longest interval after which an increase in amplitude of the response to the threshold stimulus took place. In some experiments, to determine the phase of exaltation, instead of a single testing stimulus a series of 3 such stimuli was applied (Fig. 2). In this case a small increase in the first testing action potential led to a marked increase in the subsequent potentials, thereby emphasizing the general picture of change in the testing response. As a result, the duration of the phase of exaltation could

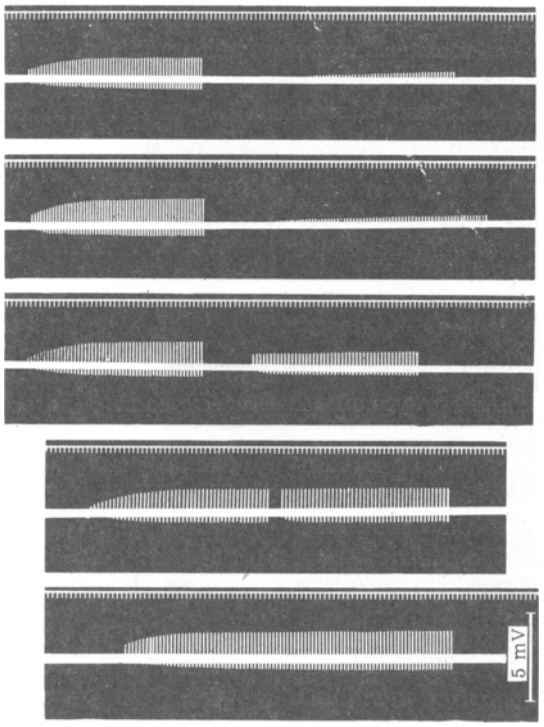


Fig. 3. Change in amplitude of testing action potentials (second volley) of altered nerve depending on duration of interval after conditioning stimulation for 1 sec (first volley). Duration of each volley 1 sec. Frequency of stimulation 50/sec.

be determined more accurately, especially at its end, when it became smaller and smaller and disappeared. The investigation showed that in every case when there was a successive increase in amplitude of the action potentials during repeated responses, the threshold of excitability after a single stimulation was depressed, i.e., a phase of exaltation occurred; its duration was very long, averaging 154.7 ± 10.1 msec and, in individual experiments, 500 msec or more. As might be expected [2, 7], the long duration of this phase of exaltation corresponded to a similar duration of the after-depolarization potential. After stimulation for 1 sec at a frequency of 50/sec (Fig. 3), the duration of after-depolarization and of the phase of exaltation was not very substantially altered, but it was nevertheless shortened slightly, on the average by 9.6 ± 1.4%.

These results thus show conclusively that the increase in amplitude of the response during repetitive stimulation of the nerve trunk correlates with the existence of a prolonged and well marked phase of exaltation, and of the depolarization responsible for it.

Clearly the increase in response of the nerve trunk to repetitive stimulation is the result of successive recruiting of new fibers, not excited by the preceding stimuli, into the response. However, it is difficult to give any further interpretation of this fact, because it cannot be explained by the summation of local potentials at the point of application of the stimulus, since augmentation of the responses was observed when the intervals between the stimuli were very long (over 500 msec) and, by contrast, they were absent when the intervals were short (below 2.5 msec).

It was pointed out above that this phenomenon is clearly related to the development of after-depolarization of the membrane. However, it must be asked how after-depolarization of some fibers can evoke increased excitability in others. The simplest explanation of this effect would apparently be to attribute it to the action of "local currents," bringing about interaction between the nerve fibers during the spread of spikes [9]. However, in the period of slowly developing after-depolarization, the local currents must be very small, for the membrane of the whole fiber is more or less depolarized (the potential gradient along the membrane is very low). It therefore seems more likely that the prolonged after-interaction between the fibers is due to the accumulation of $K^+$ ions in the interstitial spaces [6, 12]. An increase in the intercellular concentration of these ions leads to depolarization of the membrane and, as a result of this, to a lowering of the threshold of excitability both of the directly excited fibers and of their neighbors.

This or a similar mechanism of an increase in excitability could also explain certain forms of synchronization in both the peripheral and the central nervous system [1]. The electrical and chemical processes taking place in single structural units of the nervous system must evidently have a stronger and wider influence on the functional state of neighboring units than is usually considered.

## LITERATURE CITED

1. N. Yu. Belenkov, in: Current Problems in Electrophysiology of the Central Nervous System [in Russian], Moscow (1967), p. 21.
2. L. L. Katalymov, Fizol. Zh. SSSR, No. 1, 26 (1970).
3. D. G. Kvasov and A. I. Naumenko, Fiziol. Zh. SSSR, 19, 1014 (1935).
4. D. G. Kvasov, Trud. Fiziol. Nauch.-Issled. Inst. Leningrad Univ., No. 18, 101 (1937).

5. V. S. Markin, Biofizika, No. 1, 120 (1970).
6. M. Cohen, H. Gershenfeld, and S. Huffler, J. Physiol. (London), 197, 369 (1968).
7. H. T. Graham, Am. J. Physiol., 111, 452 (1935).
8. H. H. Jasper and A. M. Monnier, J. Cell Comp. Physiol., 11, 259 (1938).
9. B. Katz and O. Schmitt, J. Physiol. (London), 97, 471 (1940).
10. A. S. Marrazzi and R. Lorente de No, J. Neurophysiol., 7, 83 (1944).
11. T. Otani, Jap. J. Med. Sci., Series III (Biophysics), 4, 355 (1937).
12. A. Shanes, J. Physiol. (London), 134, 795 (1951).