EFFECT OF THE ELECTRICAL POLARIZATION OF MOTOR NERVE ENDINGS AND THEIR ABILITY TO CONDUCT RHYTHMIC IMPULSES

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Investigations of the mechanism of the pessimal block during the transmission of nervous impulses through the myoneural junction have demonstrated the complex nature of this phenomenon. Besides the changes arising in the postsynaptic formations, presynaptic changes also play an essential role in Vvedenskii's "pessimum" [4-7,12,13]. The elucidation of the nature of the presynaptic changes during the passage of fast impulses through the ending may result from the study of the changes in the functions of the presynaptic endings during changes in their electrical polarization [8-11,13,14], which may cause considerable modification to the transsynaptic action of the ending. The effect of depolarization and hyperpolarization of the terminal ramifications of the motor axon on the end-plate potentials (EPP) of a muscle fiber evoked by rhythmic nerve impulses has been investigated.

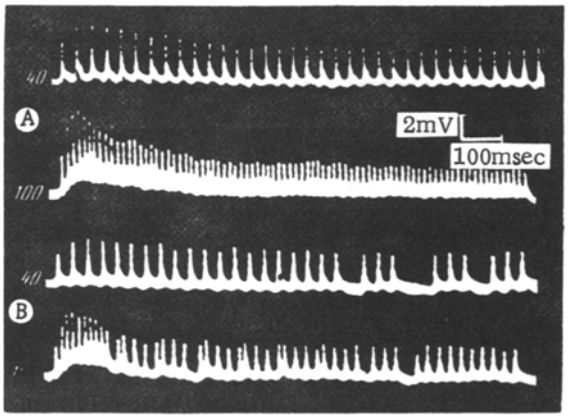

Fig. 1. Effect of depolarization of end plates on EPP generated by rhythmic pulses. A) background; B) presynaptic depolarization by current of a strength of 18 μA. The numbers at the beginning of each oscillogram denote the frequency of stimulation.

EXPERIMENTAL METHOD

Rhythmic stimulation was provided by a rectangular pulse generator with radio-frequency output. The frequency of rhythmic stimulation varied from 20 to 200 pulses/sec. Tetanization lasted for 1 sec, and the interval between series of stimuli was 1-2 min.

EXPERIMENTAL RESULTS

In ordinary conditions, in response to rhythmic stimulation with a frequency of 20-200 pulses/sec, an EPP was recorded from the synaptic region of the muscle fiber, the amplitude of which first increased and then fell gradually until it reached a relatively constant level. The effect of facilitation (an increase in the amplitude of the first EPP) and the rate of fall of the amplitude increased with an increase in the frequency of stimulation.

Stimulation with a frequency of over 200 pulses/sec led to the omission of individual EPPs in accordance with the all or nothing principle, indicating the development of a block in the presynaptic nerve endings (presynaptic block). In some preparations a presynaptic block also appeared during stimulation with lower frequencies (150 pulses/sec).

During depolarization of the nerve endings a presynaptic block appeared at all frequencies of stimulation (Fig.1). No regular pattern could be detected in the order of omission of the individual EPPs. At the beginning of a tetanic series, when depolarization of the ending was insignificant, a variable number of impulses passed without loss, and omissions appeared only later. With an increase in the strength of depolarization only one or a few impulses from each series could pass through the synapse.

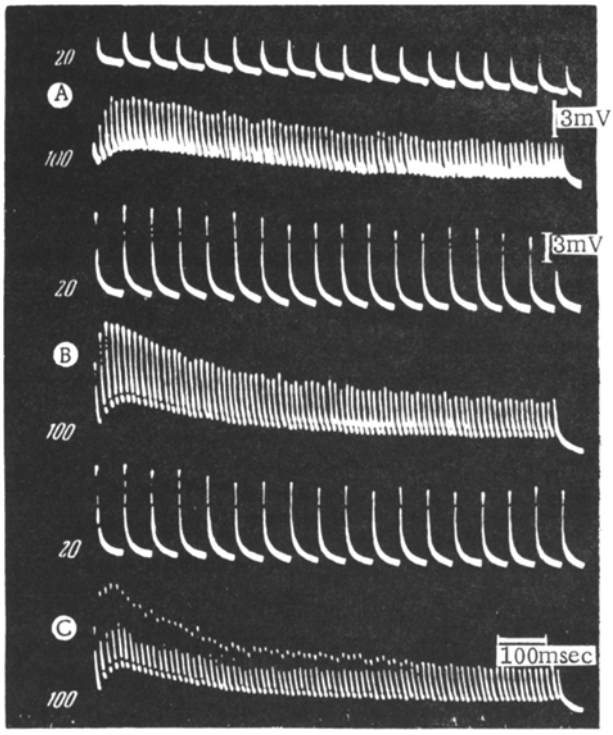

Fig. 2. Effect of a hyperpolarizing current on EPP during rhythmic stimulation. A) background; B, C) EPP 2 and 3 min respectively after beginning of hyperpolarization. Remainder of legend as in Fig. 1.

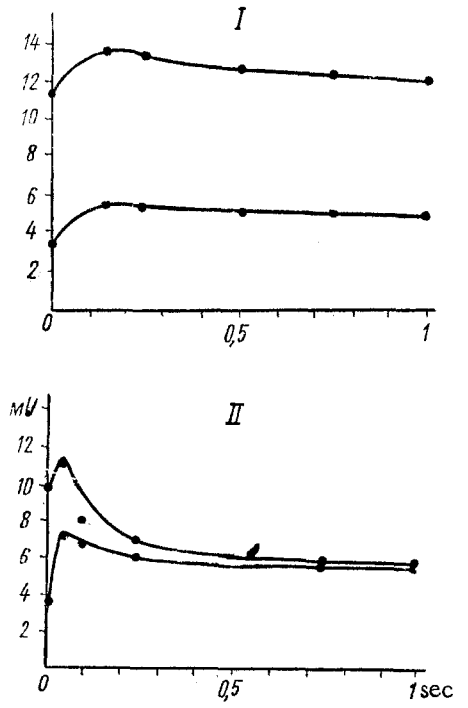

Fig. 3. Decrease in amplitude of successive EPPs during stimulation at a frequency of 1-20 pulses/sec (I) and 100 pulses/sec (II). Lower curve) EPP without polarization; upper curve) during hyperpolarization of nerve ending with current of 13 μA.

The presynaptic block disappeared after switching off the current. If the depolarization was considerable (20-25 μA) and prolonged (up to 5-7 min), before and after switching off the current omission of EPPs could be observed for 1-2 min longer when high frequencies of stimulation were used (100-150 pulses/sec). It is possible that this depolarization of the nerve endings caused an outflow of potassium ions in the region of the nerve endings, capable of depolarizing their membrane for a definite period of time after switching off the current, and leading to presynaptic block.

Recordings of the action currents from the nerve trunk at the point of entry into the muscle showed that when a current strong enough to cause the development of a presynaptic block passed, their amplitude and frequency remained essentially unchanged.

Hyperpolarization of the motor nerve endings increased the amplitude of the EPP severalfold (Fig. 2). At low frequencies of stimulation (20 pulses/sec) the response to each pulse of a tetanic series had an increased amplitude. The increase in amplitude was dependent on the duration of action of the current; it reached a maximum, as in the case of the single responses, at the end of the 3rd minute. At high frequencies of stimulation (100 pulses/sec) the amplitude of the responses to pulses from the hyperpolarized ending fell much more rapidly than normally, and at the end of the 1st second it had decreased to its initial level (Fig. 3). A slight decrease (compared with normally) was observed in the facilitation of myoneural transmission, especially for low frequencies of stimulation. After switching off the current, the amplitude of the responses gradually returned to their initial level.

In order to discover what changes take place in the presynaptic block during hyperpolarization of the nerve endings, its development was stimulated by increasing the concentration of potassium ions in the medium surrounding the presynaptic terminals. The hyperpolarizing current was then switched on. No change in the number of omitted EPPs was observed immediately; during the continued action of hyperpolarization it fell, and in the course of 2-3 min the presynaptic block completely disappeared.

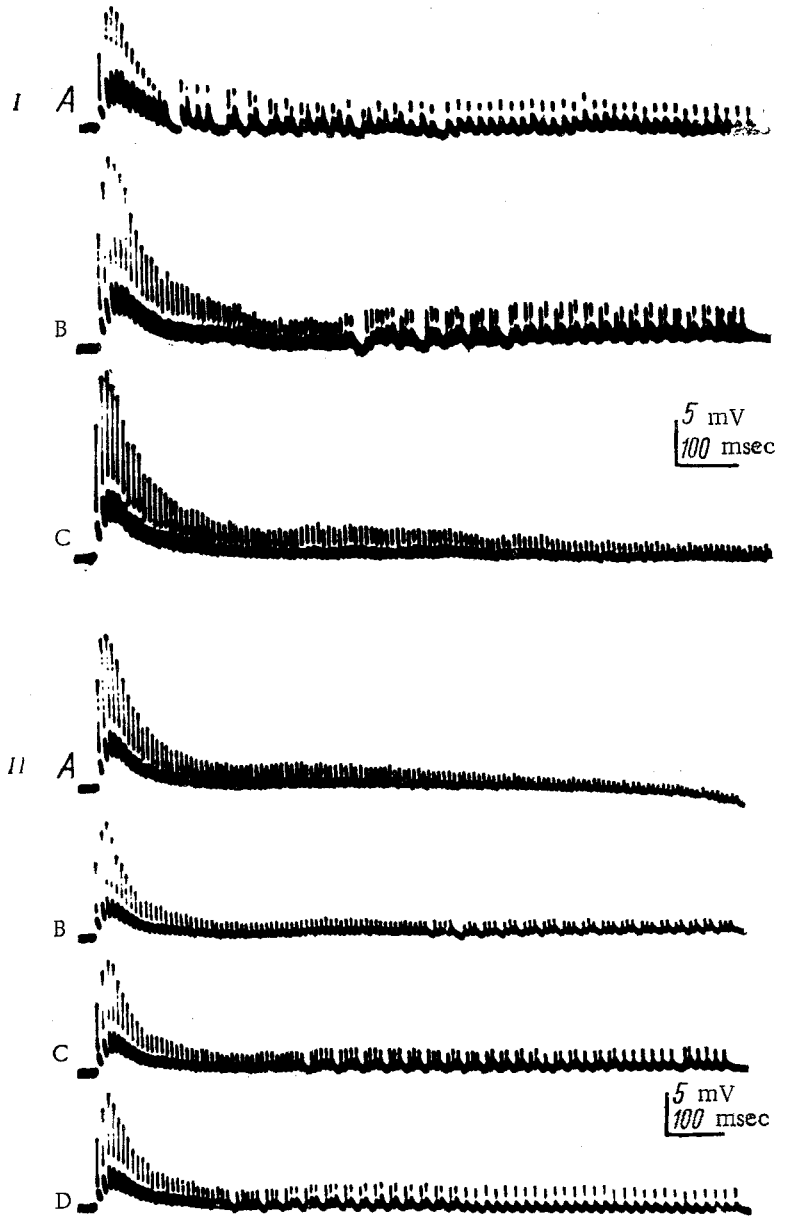

Fig. 4. I) Effect of hyperpolarization of end plates on presynaptic block of EPP caused by increased concentration of potassium ions in surrounding solution. A) EPP after increase in concentration of potassium ions to 7 mM; B) the same, after application of a hyperpolarizing current of strength 12 μA for 1 and 3 min respectively; II) changes in presynaptic block immediately (A) and 1 min (B), 2 min (C), and 3 min (D) after switching off the current.

After switching off the hyperpolarizing current, the amplitude of the responses gradually returned to its initial value and the presynaptic block reappeared (Fig. 4).

The increase in the amplitude of the EPP caused by impulses from the hyperpolarized ending during a short period of tetanic stimulation suggests that presynaptic hyperpolarization increases the amount of that part of the mediator which can be rapidly liberated by the nervous impulse (the number of synaptic vesicles concentrated in the synaptic membrane of the presynaptic ending).

The faster than normal decrease in the amplitude of these EPPs at high frequencies of stimulation and longer duration of tetanization (up to 1 sec) demonstrates that the amount of mediator to have accumulated in this part of the ending is small, and is exhausted during stimulation at a frequency of 100 pulses/sec in 0.5 sec. Subsequently equilibrium is evidently established between the secretion of mediator and the slow building up of its stocks in the synaptic membrane [15].

These results confirm the view that, besides changes in the amount of mediator secreted by each pulse during rhythmic stimulation, a total cessation of the synaptic function (presynaptic block) may also arise, and is reflected in the omission of EPPs during rhythmic impulsation and actually develops in the presynaptic endings. It may be overcome by hyperpolarization of the end plates and intensified by depolarization. This effect is not observed if the polarizing electrode is moved away from the synaptic region.

Investigations of the importance of potassium and calcium ions to the presynaptic block suggest that it is based on depolarization of the nerve endings during the passage of rhythmic nerve impulses through them, which may lead to slowing of the conduction of impulses in the endings and to interaction between the impulses themselves [2,3]. The fact that direct depolarization of the presynaptic plates facilitates, and hyperpolarization removes the presynaptic block confirms this hypothesis.

These results agree with N. E. Vvedenskii's theory [1] that the endings of the motor axon are structures with a low level of lability, and it is their function which is primarily disturbed in pessimal inhibition.

SUMMARY

A study was made of the effect produced by electric polarization of the motor nerve endings on the conduction of the rhythmic impulses through them. Increased rhythmic end-plate potentials from the hyperpolarized endings were subject to a lesser summation than in normal conditions and weakened more rapidly following prolonged rhythmic stimulation. Hyperpolarization of the nerve endings removed the presynaptic block caused by an increased potassium content in the solution surrounding the muscle. Depolarization of the nerve endings promoted the development of presynaptic blocking. These changes were observed only in local polarization of synaptic plates. A hypothesis is put forward on the nature of the changes occurring in the presynaptic endings, leading to the changes of efficacy of their transsynaptic action and to presynaptic blocking.

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