CHANGES IN THE LABILITY OF SMOOTH MUSCLE DURING STIMULATION OF THE SYMPATHETIC AND PARASYMPATHETIC NERVES

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The antagonism between the actions of the sympathetic and parasympathetic nerves of smooth muscle structures is a well known fact. In some cases the sympathetic nerve causes contraction of a smooth muscle (for example, the retractor penis muscle of the dog, the nictitating membrane of the cat), and in others it causes relaxation (for example, the musculature of the bronchi, the gastrointestinal tract, and so on). A similar dualism is observed in the action of the parasympathetic nerve. For a long time the classical concept of a pure antagonism between the sympathetic and parasympathetic systems has been inadequate for the explanation of the variety of their mutual relationships. The nerves of one system may be either inhibitory or stimulatory, depending on the region which they innervate, and on the state of the tissue on which they act. In certain doses, the action of both adrenalin and acetylcholine may be mutually potentiating [1, 5, 9, 10].

In experiments carried out on a ring of smooth muscle from the taenia coli of the guinea pig, Bulbring [7, 8] obtained results which showed a connection between stretching and the frequency of the action currents and the membrane potential of the smooth muscle fiber. He found that the effect of mediators was similar to the electrotonic influence of two direct current poles. By the action of acetylcholine or the cathode, the frequency of the action potentials is increased and the membrane potential falls; conversely, by the action of adrenalin or the anode, a rise in the membrane potential and a decrease in the frequency of action currents are observed. Thus, when the interval of time between two action currents is lengthened (under the influence of adrenalin or of stimulation of the sympathetic nerve), relaxation of the smooth muscle of the taenia coli takes place, and conversely, when the action currents are more frequent (as a result of the action of acetylcholine or of stimulation of the parasympathetic nerve), every small increment of tension following after every action current undergoes summation with others of the same kind, thereby creating a general contraction.

These findings suggest that the action of antagonistic nerves usually consists essentially of a change in the functional state, a change in the interval between the excitations in the smooth muscle cell, i.e., in other words to a change in the lability of the cell. We therefore undertook to investigate the action of the sympathetic and parasympathetic nerves on smooth muscle, and to determine the lability of the latter.

METHOD

Experiments were carried out on 27 dogs under morphine-urethane anesthesia. The test object used was the retractor penis muscle of the dog, innervated by both sympathetic (sympathetic trunk) and parasympathetic (pelvic nerve) nerve fibers. Stimulation of the sympathetic nerves causes contraction of the muscle, and stimulation of the parasympathetic nerves—relaxation. Immersible electrodes were used for the nerves, and platinum needle electrodes for stimulation of the muscle. We determined the limits of the optimal frequency and also the frequencies which led to pessimal relaxation during direct stimulation of the muscle. These values were determined before and after stimulation of the sympathetic and parasympathetic nerves, and also after giving the animal an intravenous injection of either 1% cocaine (after $1^1/_2$-2 hours) or adrenalin (after 30-40 minutes) in a dilution of 1:1000, or eserine in a dilution of 1:10,000 (after 30-40 minutes). In the experiments in which we recorded the bioelectrical activity, the muscle was attached under isometric conditions. The currents of action in response to direct stimulation of the muscle were taken by nonpolarizing electrodes to the input of a type UIPP-2 constant current amplifier with a coefficient of amplification of 50,000 and recorded on the tape of an MPO-2 8-loop oscillograph. A reduction in the magnitude of the loops of current during

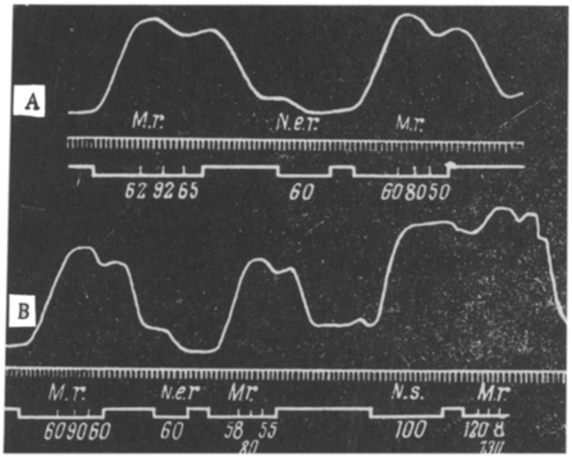

Fig. 1. Optimum and pessimum of the frequency of stimulation before and after stimulation of the sympathetic and parasympathetic nerves. Significance of the curves (from above down): myogram, time marker (5 seconds), stimulation marker. Figures — frequency of stimuli per second, M.r. — direct stimulation of the muscle; N.e.r.— stimulation of the parasympathetic nerve; Ns. — stimulation of the sympathetic nerve. A and B — tracings in two experiments.

direct stimulation was achieved by the use of a separating transformer. The index of lability was the highest frequency of the action currents and the level of their amplitude. The magnitude of the resting currents was shown in millivolts on the scale of the amplifier.

RESULTS

In the experiments using the myographic method of recording, obvious shifts were observed in the limits of the optimal and pessimal frequencies of direct stimulation of the muscle immediately after stimulation of the nerves. In all cases during stimulation of the pelvic nerve (parasympathetic nerve), the limits of the optimum and pessimum were displaced towards the lower frequencies. As may be seen from Fig. 1, A, before stimulation of the pelvic nerve, the optimal contraction developed at a frequency of stimulation of 62 imp/sec. After stimulation of the pelvic nerve, the limits of the optimum were shifted to 60 imp/sec, and the pessimum now developed at a frequency of 80 imp/sec. A different picture was observed after preliminary stimulation of the sympathetic nerve. The limits of the optimal and pessimal frequencies of stimulation in this case were displaced towards the higher frequencies. In Fig. 1, B, we show the myogram from one of the experiments. We can see that before stimulation of the nerves, the limits of the optimum and pessimum were respectively: 60 imp/sec—optimum, and 90 imp/sec—pessimum; after stimulation of the pelvic nerve these limits fell: to 58 imp/sec—optimum, and 80 imp/sec—pessimum, but after stimulation of the sympathetic nerve they were displaced towards the higher frequencies: the optimum amounted to 120 imp/sec and the pessimum developed at a frequency of stimulation of 130 imp/sec.

Investigation of the bioelectrical potentials showed that the myographically recorded changes in the functional properties of the smooth muscle were reflected in the bioelectrical picture. The magnitude of the resting current, as measured in 10 experiments, was on the average 16-25 mv. During stimulation of the sympathetic nerve a decrease was observed in the value of the resting current, by 5-7 mv. Stimulation of the parasympathetic nerve most often led to an increase of 3-5 mv in the resting current. During direct stimulation of the muscle, biphasic potentials of regular shape were recorded, which is explained by the parallel course of the muscle fibers.

Action currents of great amplitude were found at a frequency of stimulation of 50-70 imp/sec. Increasing the frequency of stimulation to 80-90 imp/sec caused a sharp fall in the amplitude of the action currents and disturbed the correlation between the waves of action currents and the frequency of the applied stimulation (Fig. 2, A). After stimulation of the pelvic nerve, the amplitude of the action currents of the muscle fell; with an increase in the frequency of stimulation above 60 imp/sec, a pessimal reaction was observed (Fig. 2, B).

Stimulation of the sympathetic nerve increased the functional properties of the smooth muscle, as shown by an increase in the amplitude of the action currents and by the widening of the limits of the optimum. A fall in the amplitude of the action currents took place only at a frequency of stimulation of 100-120 imp/sec (Fig. 2, C).

During the investigation of the action of stimulation of the sympathetic and parasympathetic nerves on the functional mobility of smooth muscle, in a series of experiments we injected drugs and, on this background investigated the functional state of the smooth muscle. Injection of 2-3 ml of a 1% solution of cocaine, or of 0.2 ml of 1:1000 adrenalin solution usually led to displacement of the limits of the optimal and pessimal frequencies of stimulation towards the higher frequencies, soon after the injection. Eserine, when injected in a dose of 2-3 ml (concentration of 1:10,000), caused a displacement of the values of optimal and pessimal stimulation towards the lower frequencies. This effect was usually apparent 20-30 minutes from the moment of injection of the eserine.

The experimental results thus show that excitation of both the sympathetic and parasympathetic nerves influences a very important index of the functional state of a muscle—its lability. In this particular case, stimulation of the sympathetic nerve brings about a displacement of the limits of the optimum and pessimum towards the higher frequencies, an increase in the amplitude and frequency of the action currents and a fall in the resting current. Excitation of the parasympathetic nerve causes the opposite effect: Displacement of the limits of the

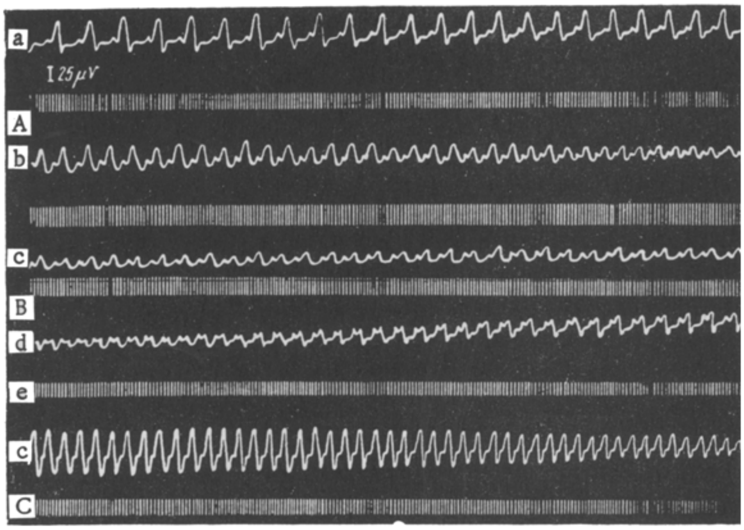

Fig. 2. Action currents of smooth muscle during direct stimulation of the muscle before and after preliminary stimulation of the sympathetic and parasympathetic nerves. A – before stimulation of the nerves: a-frequency of stimulation 50-60 imp/sec, b-frequency of stimulation 80-90 imp/sec; B – after stimulation of the parasympatheitc nerve: c-frequency of stimulation 60 imp/sec, d-frequency of stimulation 70 imp/sec; C – after stimulation of the sympathetic nerve; e-frequency of stimulation 100-120 imp/sec. Time-marker – 0.02 second. Calibration in millivolts.

optimum and pessimum toward the lower frequencies, a reduction in the amplitude and maximum frequency of the action potentials in response to direct stimulation of the smooth muscle and an increase in the resting current. Substances having a sympathotropic or parasympathotropic character act in the same way as excitation of the nerves. Thus the sympathetic nerve, causing contraction of the retractor penis muscle, and the parasympathetic nerve which causes it to relax, affect the functional mobility of smooth muscles.

Smooth muscle is known to preserve its tone in preparations deprived of nerves and ganglion cells [11] and also during the action of ganglion-blocking drugs, as shown by its tonic contraction and by spontaneous discharges of action potentials. The tonic state of the smooth muscle is probably due to changes in muscle metabolism. The level of the muscle metabolism of the body, however, is to a large extent determined by nervous influences, and mainly by the mediators of nervous influence – sympathin and acetylcholine [3,4]. Work by A. V. Kibyakov and N. G. Bohdanov [2] showed that firstly, after division of nerves, and in particular the sympathetic nerve, the tonic state of smooth muscle is not disturbed; secondly, degeneration of divided sympathetic nerves at a certain period completely abolishes its tone; and thirdly, interference with the synthesis of sympathin leads to a sharp fall in the tone of smooth muscle. It may be assumed that the action of nerves, besides their trigger action, is directed towards changing the tonic state of smooth muscle which, evidently, is effected through the constant influence of mediators, which are also liberated when no excitation of the nerves is taking place. Excitation of the sympathetic nerve by means of the mediator, sympathin, increases the lability of the smooth muscle, gives rise to an increase in the amplitude and frequency of the action potentials. Excitation of the parasympathetic nerve, in this case through the medium of acetylcholine, lowers the lability of the smooth muscle, as shown by the decrease in the amplitude and frequency of the action potentials during direct stimulation of the muscle.

The "antagonism" between the sympathetic and parasympathetic innervation of smooth muscle in all probability consists essentially of their action on the functional properties of the muscle and, in particular, on its lability.

SUMMARY

The effect of sympathetic and parasympathetic nerves of a smooth muscle—the retractor penis—was investigated. Stimulation of the sympathetic nerve extends the limits of the optimal and pessimal frequency of stimulation towards greater frequencies, the action current frequency and amplitude increase, while the value of the resting current decreases.

On stimulation of the parasympathetic nerve, the action current frequencies become decreased, their amplitude declines and the resting current rises.

A suggestion is made that the "antagonism" of the sympathetic and parasympathetic innervation of the smooth muscle apparently is due to the action exerted on the functional properties of the muscle, particularly on its lability.

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