THE EFFECT OF GANGLION-BLOCKING DRUGS ON THE CONDUCTION VELOCITY OF NERVOUS EXCITATION IN THE SYMPATHETIC GANGLIA

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(Presented by Active Member AMN SSSR V. V. Zakusov)
Translated from Byulleten' éksperimental'noi biologii i meditsiny Vol. 49 No. 3, pp. 61-64, March, 1960
Original article submitted February 19, 1959

As we know one of the fundamental characteristics of the functions of the nervous system is the velocity with which a stimulus is propagated. This factor is especially significant when applied to the interneuronal transmission of nerve impulses. In addition, as the work of V. V. Zakusov and co-workers has shown [2, 3, 5, 6, 7, 8], the amount of synaptic suppression is one of the more precise criteria for the evaluation of substances which act on the central nervous system.

Starting with this information, and continuing our attempts to elucidate the mechanism of action of ganglion-blocking substances [9, 10, 12], we undertook the present work, which is a study of the influence of ganglion-blocking agents on the conduction velocity of nervous excitation in the sympathetic ganglia.

METHOD

The experiments were performed on anaesthetized cats. The anesthetic used was either urethane (1 to 1.5 mg/kg by intraperitoneal injection) or a mixture of chloralose (80 mg/kg) with urethane (0.5 g for each animal, injected intravenously). The bioelectric potentials of the postganglionic fibers of the superior cervical and stellate ganglia were discharged through bipolar platinum electrodes. The preganglionic fibers were stimulated by successions of single squarewave supramaximal stimuli (3 to 5 per series) with an interval of 5 to 60 seconds between each stimulus, the duration of the latter being 0.1 to 0.5 milliseconds. The latent period was measured between the artifact of the stimulus and the commencement of the potential (Figs. 2a and b).

In experiments on the stellate ganglion the bioelectric potentials were discharged from the inferior cardiac nerve. All the other postganglionic fibers, as well as the 1-5 rami communicantes, were cut. The sympathetic thoracic chain was either tied or cut on a level with the 5th or 6th ganglion. Thus the stellate ganglion was completely isolated from any influence whatever on the central nervous system. The blood supply was meanwhile maintained. The stimulating electrodes were placed on the thoracic sympathetic chain, usually between the 3rd and 4th, or 4th and 5th ganglia. Artificial respiration was used in the experiments.

We recorded the potentials of the postganglionic fibers of the superior cervical ganglion when the peripheral segment of the cervical sympathetic trunk (presynaptic fibers) was submitted to electrical stimulus.

Among the ganglion-blocking substances tested were tetraethylammonia (0.5 to 5 mg/kg), hexonium (0.5 to 7 mg/kg), pentamine (0.5 to 10 mg/kg), and mecamine (0.5 to 6 mg/kg). In addition, for purposes of comparison, experiments were performed with novocain (15 to 25 mg/kg) and barbamyl (10 to 20 mg/kg). The substances were injected into the femoral vein.

RESULTS

The results obtained indicate that all the ganglion-blocking substances which we tested decrease the conduction velocity of sympathetic ganglia excitation. This applies equally to the superior cervical and the stellate ganglia. Any alteration in the latent period, consequent on a considerable reduction in the amplitude of the bioelectric potentials, was usually expressed in the form of an increase of 0.5 to 2 milliseconds.

It must be stated that, in all the experiments, only supramaximal stimulation was applied. Comparison of results was thereby noticeably simplified, quite apart from the fact that supramaximal stimulation provided the most reliable conditions. It did not appear to be worthwhile to apply different amplitudes of stimulation in the presence of the substances under test, as an increase in the strength of stimulus from a liminal to a supramaximal value was not accompanied by any noticeable change in the latent period. Evidently the initial part of the biological currents (before which the latent period is measured) is the result of the activity of neurones with the least excitability discharging with liminal stimulation of the preganglionic fibers.

Changes in the latent period induced by ganglion-blocking agents may be considerably greater than those

mentioned earlier. Thus, as shown in Fig. 1, the conduction time of the stimulus in the superior cervical ganglion is increased by 4 milliseconds under the influence of tetraethylammonia (1 mg/kg). A marked decrease in the amplitude of the biological currents was observed simultaneously.

Analogous results are shown in Table 2. Following injection of hexonium 5 mg/kg in divided doses spread over 25 minutes (1+1+1+2 mg/kg) the conduction time in the stellate ganglion increased by 3.7 milliseconds. At the same time the potential noticeably decreased.

However, an increase in the latent period takes place only up to a certain limit. Thus, in our investigations into ganglion-blocking drugs, the latent period did not extend beyond 5 milliseconds. A further increase in the dose led to complete block of ganglionic transmission.

In no experiment was there observed a reduction in the latent period, even with small doses.

Having established the possibility of ganglion-blocking agents having a retarding effect on the conduction velocity of excitation in the sympathetic ganglia, we thought that it would be interesting to study other substances which showed marked ganglion-blocking properties. We therefore investigated novocain and barbamyl. These substances were selected because experiments had

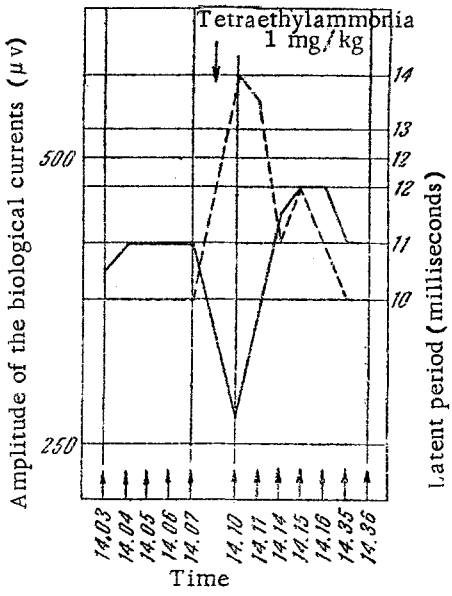

Fig. 1. Influence of tetraethylammonia on conduction velocity of excitation in the superior cervical ganglion. Continuous line—amplitude of postganglion potentials; broken line—latent period (period between the artefact of excitation and onset of potential; vertical arrows ( ) above the time scale—single supramaximal stimuli.

shown that they definitely depress the transmission of nerve impulses in the sympathetic ganglia [1, 9, 11, 15]. It was established that both compounds have a depressive effect on the velocity of propagation of stimuli. Barbamyl (15 mg/kg) and novocain (25 mg/kg) noticeably increased the transmission time (Fig. 3). This effect, in the case of both substances, was always accompanied by a decrease in the amplitude of the biological currents. Pessimol* retardation developed noticeably earlier than in the control.

It follows from the data shown that ganglion-blocking substances lower the synaptic velocity in the sympathetic ganglia. The latent period is usually increased by 1 to 3 milliseconds, which is quite considerable if one takes into account that the true synaptic suppression for the group of cells with the lowest liminal excitability is

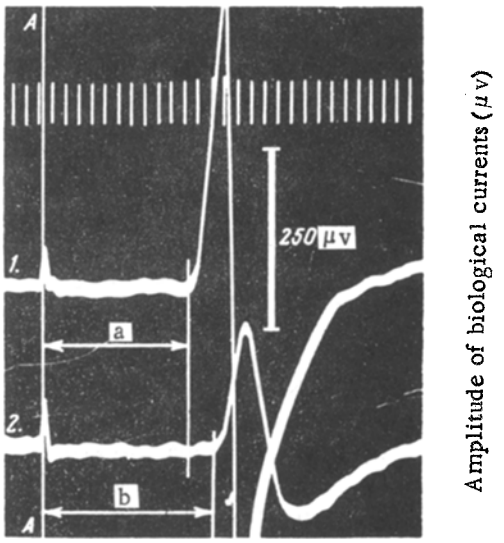

Fig. 2. Biological currents of postganglionic fibers (stellate ganglion). 1) Before; 2) after injection of hexonium 5 mg/kg (divided doses over a period of 25 minutes 1 + 1 + 1 + 2 mg/kg); line A - A, corresponding to the time of stimulation of the preganglionic fibers; a, b—values of the latent period before and after administration of hexonium; vertical lines in the upper part of the figure—time (one division = 2 milliseconds).

2 to 3 milliseconds [13, 14, 16]. An increase in the latent period is evidently connected with the fact that the ganglion-blocking substances extend the time of development of synaptic potential up to a critical value related to the discharge of the ganglionic cells. Consequently we may suppose that the transition of the local stimulus into a diffuse stimulus becomes more difficult. This latter effect must obviously be considered one of the fundamental manifestations of the action of ganglion-blocking substances.

Changes in the velocity of interneuronal transmission, observed when ganglion-blocking substances were applied, are usually accompanied by a noticeable decrease in the amplitude of the biological currents of the postganglionic fibers. In addition, as shown earlier [9, 10, 12], the substances which we tested lower the functional mobility (lability) of the superior cervical ganglion, which can be judged by the displacement of the pessimal reaction towards the lower frequencies. Evidently, in-

*Transliteration of Russian - Publisher's note.

crease in synaptic retardation also testifies to lowering of lability, the fundamental character of which is the

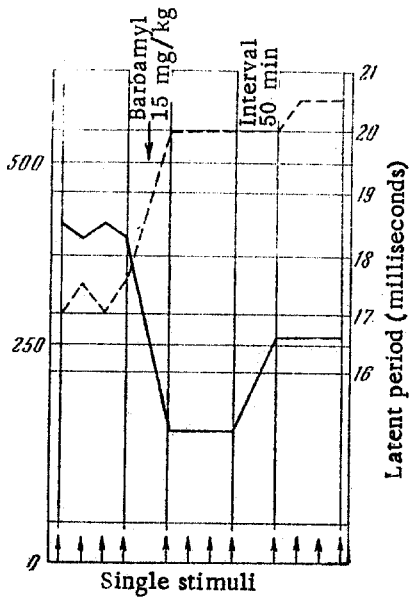

Fig. 3. Influence of barbamyl on conduction velocity of excitation in the stellate ganglion. Continuous line amplitude of bioligical currents of postganglionic fibres; broken line latent period, intervals between stimuli of each series (of 4 stimuli) 5 seconds; the time of stimulus is indicated by the vertical arrows ( ).

"velocity of those elementary reactions which accompany functional activity" (N. E. Vvedenskii [4]).

In addition to ganglion-blocking agents, barbamyl and novocain were investigated. This part of the work was done to show whether a change in the value of the latent period is also produced as a general rule by other pharmacological groups which have the ability to depress ganglionic transmission.

We established in our experiments that barbamyl and novocain, in addition to the ganglion-blocking agents, increase the latent period, at the same time noticeably decreasing the lability of the ganglionic neurons and reducing the amplitude of the postganglionic potentials.

Thus, from the facts discovered, we can conclude that a decrease in the conduction velocity of ganglionic excitation may be regarded as a general manifestation of the action of substances which possess gangliotic properties, regardless of the mechanism of their depressive influence.

SUMMARY

Experiments were performed on cats under urethane-chloralose anaesthesia. The author studied the effect of ganglioblocking drugs, novocain and barbamyl on the condition velocity (latency) of excitation in the superior cervical and stellate ganglia. Discharges from postganglionic fibers were recorded in response to a single supramaximal electric stimulation of the preganglionic trunk.

All the preparations investigated viz., tetraethylammonium (0.5 - 10 mg/kg), hexonium (0.5-7 mg/kg) pentamine (0.5-10 mg/kg), mecamine (0.5-6 mg/kg), novocain (15-20 mg/kg) and barbamyl (10-20 mg/kg) provoked a lengthening of the interval between the artifact of the exciting stimulus and the response discharge by 0.5-4 milliseconds, which was parallelled by a decrease of the discharge amplitude. Reduction of the synaptic conduction velocity in the ganglia occuring under the effect of the substances under investigation is regarded as a consequence of decreased functional mobility of the ganglionic neurons; it is viewed as a general manifestation of the action of gangliotics, irrespective of the mechanism of their depressive effect.

† Original Russian pagination. See C. B. translation.

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