PHARMACOLOGY

THE EFFECT OF BODY TEMPERATURE ON TRANSMISSION OF EXCITATION IN THE SUPERIOR CERVICAL GANGLION AND THE ACTION OF GANGLION-BLOCKING PREPARATIONS

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Artificial lowering of body temperature has recently attracted much attention from surgeons who have been using hypothermia in certain operative procedures. Various ganglion-blocking agents are used in conjunction with hypothermia. It is postulated that these measures lower the metabolism and the general reactivity of the organism [8]. It is therefore important to investigate autonomic ganglionic transmission of excitation and the action of substances which depress this transmission under conditions of general cooling.

EXPERIMENTAL METHODS

Experiments were performed on cats under urethane anesthesia. The effect of hypothermia on transmission of excitation in the superior cervical sympathetic ganglion was studied. The preganglionic sympathetic trunk was stimulated by square-pulse stimuli from an electronic stimulator; the duration of the stimuli was 0.1-0.2 m sec with constant amplitude and variable frequency for each experiment. Contraction of the nictitating membrane was recorded on a smoked drum kymograph. Increasing the frequency of stimuli led to partial relaxation of the nictitating membrane, which corresponded to the least reaction. Return to the initial, optimal, frequency of stimulation restored the mechanogram to its former magnitude. Using the oscillographic method of recording, the ganglion action potentials were led off from the postganglionic fibers through a single channel balanced A. C. amplifier and recorded by means of an oscillograph. The biopotentials were photographed during stimulation at 2-3 second intervals. The state of ganglionic transmission of excitation was judged by the maximal rhythm reproducible without transformation and by the time during which a decrease of biopotential amplitude took place. The animals were cooled in a double-walled metal bath filled with water at 3-4°. The rectal temperature was measured with a mercury thermometer. In some of the experiments cats decerebrated at the collicular level were used. No perceptible difference could be demonstrated between urethane-anesthetized and decerebrate animals, which corresponds to the data of M. G. Larrabee and I. M. Posternak [9], who showed that urethane in narcotic doses did not affect transmission of excitation in sympathetic ganglia.

RESULTS

Lowering the body temperature to 26-25° did not exert any appreciable effect on contraction of the nictitating membrane. The magnitude of the mechanogram usually remained unchanged. The least reaction often appeared during the initial period of cooling (35-29°) at higher frequencies of rhythmic stimulation than was the case under normal conditions. Further lowering of body temperature produced diminution of lability which was expressed in a shift of the least reaction towards lower frequencies. When the body temperature dropped below 23-20°, however, the lability and magnitude of nictitating membrane contraction were markedly lowered. If

cooling was continued it was possible to observe complete absence of contractions regardless of the frequency of stimulation. In some experiments the lowering of lability and amplitude of the nictitating membrane contractions occurred as early as 27-33°. Warming of the animal led to restoration of the mechanogram value.

Oscillographic records showed that the amplitude of the action potentials at low rates of rhythmic stimulation (5-10 cps) did not change substantially with the onset of hypothermia. At the same time it was possible to observe a progressive diminution in the capacity of the ganglion to reproduce without transformation the higher rhythms of stimulation (20-50 cps; Fig. 1). Diminution of lability was expressed by the more rapid decrease in the amplitude of the electric potentials than in the normal. When the body temperature reached 27-25° the frequency of the biopotentials recorded from the ganglion did not exceed 10-15 cps. the latent period of biopotentials synchronous with the stimulation became markedly longer.

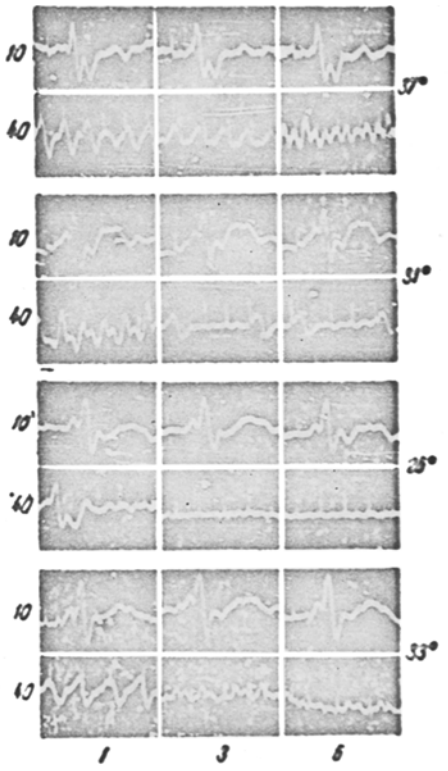

Fig. 1. The effect of body temperature on postganglionic fiber potentials. Figures at left (in this and other figures) refer to frequencies of stimulation of the preganglionic trunk (in cps).*

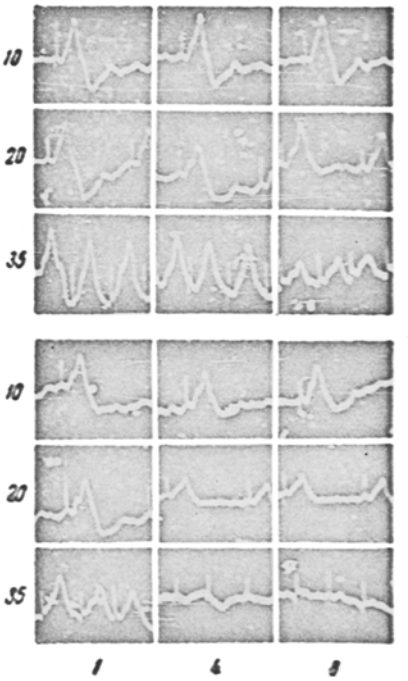

Fig. 2. The effect of body temperature (36°) on the ganglion-blocking action of hexonium. Arrow marks administration of hexonium.

Oscillographic records failed to show a phase of increased lability [illegible]seen in the experiments with recording of the nictitating membrane contractions. These differences may be explained by the fact that lowering of temperature evokes an increase of tonus in smooth muscle [11], which tends to prevent its relaxation despite the development of the least reaction in the ganglion cell.

It must be noted that cooling to 33-29° often produced considerable increase of the slow negative component of the bioelectric potentials recorded from the postganglionic fibers. These changes were particularly apparent when the frequency of stimulation did not exceed 10-15 cps, . under those conditions when the true form of the biopotentials could still be observed [2].

The data obtained correspond with those available in the literature. Thus, D. W. Bronk and R. Pamphrey [3] establishes that on lowering the temperature progressive lowering of synchronous electric activity in the stellate ganglion takes place. W. W. Douglas and J. M. Ritchie [5] did not observe any change of excitation in the superior cervical ganglion of rabbit at low rates of stimulation carried out with cooling.

* Transliterated from Russian -- probably hexamethonium.

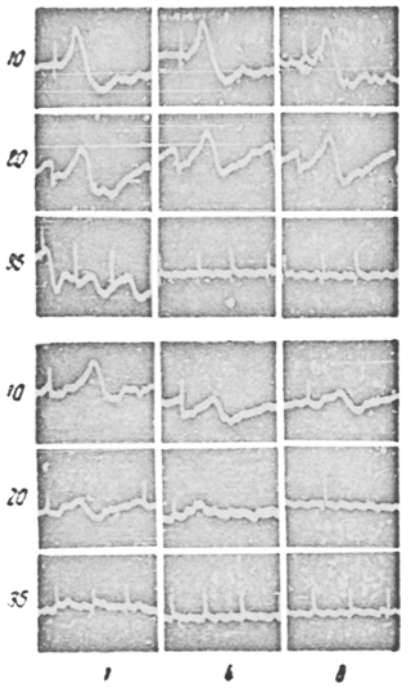

Fig. 3. The effect of body temperature (25°) on ganglion-blocking action of hexonium. Arrow marks administration of hexonium.

Studies on the effect of hypothermia on the action of ganglion-blocking agents included investigation of sparteine sulphate, tetraethylammonium iodide and hexonium. As was shown by Kharkevich [1], sparteine and tetraethylammonium hamper transmission of excitation from the ganglion first of all at high frequencies of stimulation. Analogous results were obtained in the present work with hexonium.

The blocking effect of the substances being studied increased as the body temperature was lowered. This was expressed in the mechanograms by lowering of the height of contraction in cooled animals by doses of ganglion-blocking agents which, under normal conditions of body temperature, caused only a drop in lability without any effect on the size of the mechanogram at optimal frequency of stimulation. However, relaxation of the nictitating membrane corresponding to the least reaction was often less pronounced at low temperature.

Oscillographic records showed that the decrease in amplitude of the biopotentials following administration of hexonium, sparteine and tetraethylammonium was more pronounced the lower the body temperature (Figs. 2 and 3). It should be stressed that the increase in blocking action only became apparent when the body temperature was lowered to 27-26°. Complete abolition of excitatory transmission at 24°, as shown by the oscillographic records, required doses of hexonium, sparteine and tetraethylammonium which were $1\frac{1}{2}$-2 times smaller than those at 36-37°. Analogous data were obtained by Taddei and Mosetti [12] using arfonad, a ganglion-blocking agent. Restoration of excitation transmission in cooled animals occurred 2-3 times more slowly than at normal body temperature. Therefore repeated administration of the substances led to greater disturbances than at normal temperature.

There are references in the literature to the dependence on temperature of acetylcholine production and of the sensitivity to it of choline-reactive structures. However, Kostial and Vouk [7] found, in their experiments on the isolated rat cervical ganglion, that the amount of acetylcholine on stimulation of the preganglionic trunk did not alter appreciably at temperatures within the range of 40 to 20°. Pascoe [10], using the same experimental preparation, did not find any changes of the depolarizing action of acetylcholine on altering the temperature from 38 to 3°.

In the present experiments with intravenous administration of acetylcholine no substantial differences in nictitating membrane contractions could be detected when comparing normal and cooled animals. It can therefore be suggested that the diminution of lability evoked by hypothermia does not depend on impairment of the synthesis and destruction of acetylcholine. As shown by biochemical studies, the consumption of glucose and oxygen by the sympathetic ganglion drops sharply with lowering of temperature [4, 6]. Evidently, it is the decreased intensity of metabolic processes which leads to lowering of the functional activity of ganglion cells as expressed by the shift of the least reaction towards lower frequencies.

SUMMARY

Decrease in lability in the upper cervical ganglion which was manifested by the shift of pessimum towards low frequencies was observed in cats when their body temperature was gradually decreased from 37°C to 25-24° C. The response to rare (optimal) rhythms of stimulation was almost unchanged. The effect of the substances, which block the transmission of excitation in the ganglion was almost unchanged in cooling from 37° C to 33-31° C, but with lower temperatures of the body their effect was enhanced. If the body temperature is brought back to normal the functions of the ganglion were restored.

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