RECEPTOR FUNCTION OF THE SUPERIOR SERVICAL SYMPHATHETIC GANGLION

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The question of the receptor function of the autonomic ganglia has frequently been discussed in the literature. Besides histomorphological data [1, 10, 11, 13, 14, 16, 17] reports have been published describing the results of physiological investigations [3-5, 8, 12] indicating the presence of an afferent innervation of the sympathetic ganglia. By administration of physiologically active substances to the perfused ganglia of the sympathetic chain and the solar plexus, some investigators [3, 4, 8, 21] have observed reflex responses of the arterial pressure and respiration and contractions of the skeletal muscles.

The present paper describes the results of experiments in which, during the study of the effect of chemical mediators of synaptic transmission (acetylcholine, histamine) and neurotropic substances possessing anesthetic and anti-mediator activity (allo-ocimene [2, 19, 21], diethylaminoethanol [22, 31], and xylocaine [20, 22]) on the sympathetic ganglion, it was found that the function of this ganglion does not consist entirely of centrifugal effects.

EXPERIMENTAL METHOD

The superior cervical sympathetic ganglion of a cat anesthetized with urethane was isolated from humoral connection with the rest of the body leaving its nervous connections intact and was perfused [6] with Ringer–Locke solution without addition of eserine [18, 20, 22, 23]. While the ganglion was being perfused, it was irrigated in order to maintain a constant temperature and to prevent absorption of the tested substances into the blood stream [18]. The respiration, blood pressure (femoral artery) and contractions of the nictitating membrane on both sides were recorded during the action of the chemical substances on the ganglion and during stimulation of the preganglionic sympathetic trunk with an induction current with a frequency of 20 cps and a strength 50 mm above threshold, for 5 sec. The voltage of the current in the primary circuit was 2.5 V. The appearance of generalized motor reactions was noted visually, but in some cases these reactions were noted during recording of the reactions of the nictitating membrane. Completeness of isolation of the ganglion from the vascular system was verified by investigation of the perfusion fluid for erythrocytes and by perfusion of the ganglion at the end of the experiment with methylene blue solution. Altogether 30 experiments were carried out in which the number of injections of substances into the fluid perfusing the ganglion was about 90, the number of injections into the blood vessels was 15, and the excitability of the ganglion to the induction current was measured more than 300 times.

EXPERIMENTAL RESULTS

Injection of acetylcholine and histamine (1-20 μg) produced reactions not only of the effector organ, but also of the arterial pressure and respiration, and in some cases generalized motor reaction. Their latent period ranged from 1-20 sec. Acetylcholine led mainly to depressor reactions of the blood pressure. Injection of histamine immediately after acetylcholine and in the same dose caused a pressor reaction of the blood pressure. Injection of both substances stimulated respiration and caused the appearance of a reaction of the effector organ–a contraction of the nictitating membrane (Fig. 1).

When acetylcholine was applied to the ganglion together with allo-ocimene–an analogue of the side chain of vitamin A–the depressor reaction of the arterial pressure and the increased respiration caused by administration of acetylcholine were considerably weakened. At the same time the reaction of the nictitating membrane to chemical and electrical stimulation disappeared. In the latter case, the muscle

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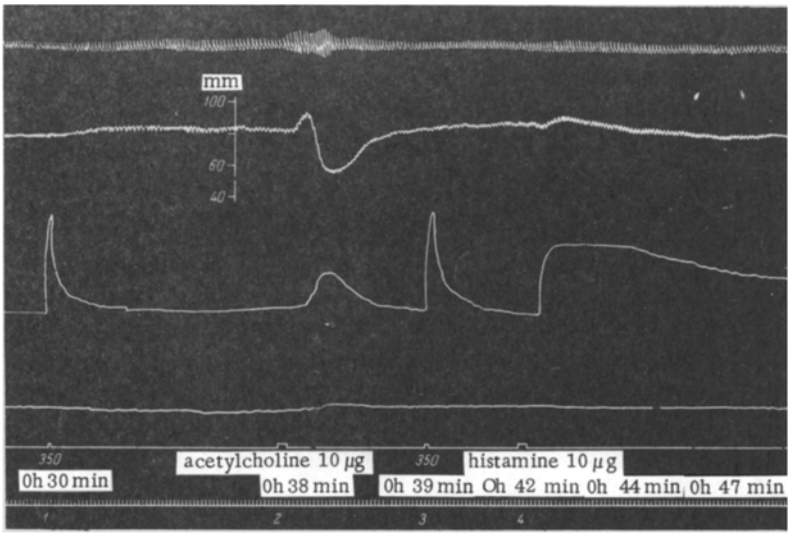

Fig. 1. Effects of inection of equal doses of various chemical stimulants—acetylcholine and histamine—into the perfusion fluid on the superior cervical sympathetic ganglion. Perfusion of the left ganglion. From bottom to top: time marker with interval 5 sec; marker of stimulation of ganglion; reaction of right and left nictitating membranes; reaction of blood pressure, respiration. 1 and 3) Responses of nictitating membrane to stimulation of the preganglionic sympathetic trunk by an induction current with a strength of 50 mm above the threshold value for 5 sec; 2) injection of acetylcholine (10 μg); 4) injection of histamine (10 μg).

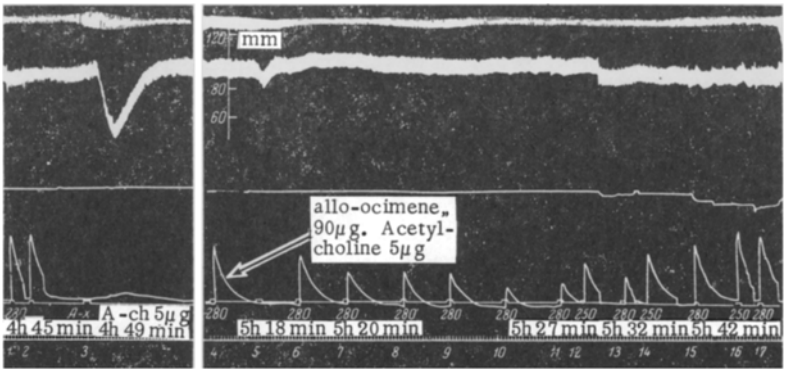

Fig. 2. Abolition of reflex responses of the arterial pressure, respiration, and nictitating membrane to the action of chemical (acetylcholine) and electrical (induction current) stimuli by allo-ocimene. Perfusion of the right ganglion. From bottom to top: the same as in Fig. 1; 1,2,4,6-11,13,15-17) the same as in Fig. 1 (12, 14, 16—strength of current 80 mm above threshold); 3) injection of acetylcholine alone in a dose of 5 μg; 5) injection of the same dose of acetylcholine together with allo-ocimene in a dose of 90 μg.

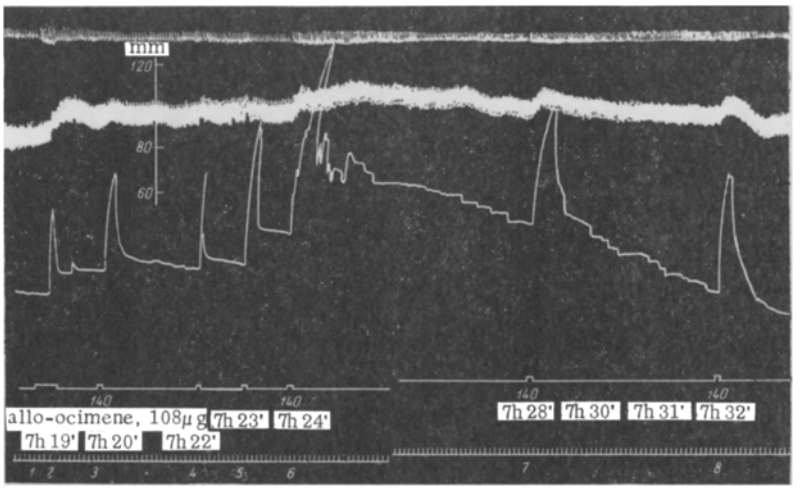

Fig. 3. Reflex responses of arterial pressure, respiration, and muscle of the nictitating membrane following administration of allo-ocimene to the ganglion. Perfusion of the left ganglion. From bottom to top: time marker with interval 5 sec; marker of time of stimulation of ganglion; reactions of left nictitating membrane; reaction of blood pressure; respiration. 1) Injection of allo-ocimene in a dose of 108 μg; 2-8) the same as in Fig. 1 [6) simultaneously with contraction of the nictitating membrane a generalized motor reaction took place].

tone of the nictitating membrane also was lowered (Fig. 2). A further increase in the dose of allo-ocimene completely abolished these reactions. In some cases the responses of the blood pressure even became pressor in character and were accompanied by a reaction of contraction of the nictitating membrane on the contralateral side.

Injection of allo-ocimene in a dose of 10 μg had no effect on these reactions. A large dose of this compound (90-100 μg) caused a pressor reaction of the arterial pressure, an increase in respiration, a contraction of the nictitating membrane, during which increased excitability of the ganglion to the electrical stimulation also was observed. A generalized motor reaction also took place at this time (Fig. 3). Consequently, allo-ocimene itself has the property not only to cause reflex excitation of the effector organ, but also to act centripetally.

Injection of allo-ocimene both intravenously and intra-arterially in doses of between 5 and 300 μg caused a depressor reaction of the blood pressure.

Preliminary perfusion of the sympathetic ganglia with novocaine [3-5, 8] abolished or diminished the reaction of the arterial pressure and respiration to acetylcholine. In the present experiments this result was observed when not only allo-ocimene, but also xylocaine and diethylaminoethanol—a hydrolysis product of novacaine—was injected into the ganglion along with acetylcholine. In these circumstances abolition of the reaction of the nictitating membrane to the mediator also was observed [22]. Injection of diethylaminoethanol alone caused no decrease of the blood pressure. Novocaine and xylocaine in doses of 1-20 μg did not change or raise the arterial pressure, i.e., they produced a reaction opposite in sign to the mainly depressor effects of acetylcholine. The local anesthetics frequently prolonged the latent period of the reaction of contraction of the nictitating membrane to this mediator considerably.

Divergence of the amplitudes of the responses of the effector organ and the central nervous structures taking part in the formation of the reflex responses of the arterial pressure and respiration was noted. For instance, depression or total absence of the reactions of the nictitating membrane to repeated administration of mediator to the ganglion was not accompanied by a change in the magnitudes of the blood pressure and respiration responses. Conversely, these responses were absent when marked reactions of the nictitating membrane were found.

Divergence of the responses of the effector organ to admistration of mediators and to electrical stimulation of the ganglion was also found. The experiments showed that the local anesthetics were capable of acting on different efferent substrates of the ganglion, each of which was adapted for stimulation of a different nature.

The results obtained demonstrate the reflex character of the phenomena observed. Evidence against the effecrent sympathetic nature of the vasomotor and respiratory effects in the experiments described above is given by reports [25, 26] of the absence of these reactions during stimulation of the cranial end of both the preganglionic and the postganglionic sympathetic trunk. Fibers of parasympathetic nature are often found in these trunks [25, 28]. The results of the present experiments justify similar conclusions.

On the other hand, the experiments of I. A. Bulygin and co-workers [3-5, 8] rule out, because of appropriate division of the pathways, any participation of the ganglion nodosum, its pre- and postganglionic fibers, the postganglionic sympathetic fibers and the region of the carotid sinus in the mechanism of the central reflex reactions described above. The carotid sinus was also painted with formalin solution.

The fine vascularization of the superior cervical [29] and other ganglia of the lateral sympathetic trunk [24] has been described. However, in the superior cervical sympathetic ganglion whole groups of nerve cells lie in one capillary loop. In most cases, no contact has been found between these cells and the surrounding capillaries [9]. Often very thin ramifications of the axons are accompanied only by a very poorly developed vaso-capillary network [9]. Moreover, the problem of how the blood vessels of the ganglia are innervated remains unsolved, as B. A. Dolgo-Saburov [7] points out. It is therefore impossible to expalin the central reflex effects discovered by the action of mediators and anesthetics on the vascular network of the perfused superior cervical sympathetic ganglion. On the other hand, the results of physiological [3-5, 8, 12] and morphological [1, 10, 11, 13, 14, 16, 17] investigations are sufficient to demonstrate directly that the central reflex reactions are brought about by the existence of an afferent innervation, or in other words, that the superior cervical and the other sympathetic ganglia perform a true receptor function. In this connection the data concerning the specific biochemical systems of the receptor substrate are of great interest [15, 30].

The author reported some time ago that novocaine, while abolishing the effects of acetylcholine on the perfused superior cervical sympathetic ganglion, does not depress, but may even stimulate the cholinesterase activity of the ganglion [18, 22]. In more recent investigations [32] the anti-acetycholine effect of novocaine has been confirmed, although not accompanied in these cases by depression of cholinesterase activity. Novocaine block has been shown to be due to chemical interaction between novocaine [32] and the acetylcholine receptor protein [27, 32].

Novocaine and the other local anesthetics, which have an anti-mediator action during the transmission of information centrifugally in the ganglion, have been found to be capable of abolishing the central reflex effects of the mediator. It may be postulated that the specific biochemical systems present in the receptor structures of the sympathetic ganglion are the substratum for the competetive action of mediators not only with novocaine, but also with other local anesthetics.

If follows from the results of these experiments that mediators and anesthetics, when applied to the perfused sympathetic ganglion, produce reflex effects not only on the effector organ—the nictitating membrane, but also on the vaso-motor, respiratory, and sometimes also the locomotor centers. Hence it follows that these substances act on different substrata in the ganglion, some of which are responsible for transmission of information centrifugally, to the effector organ, and others—centripetally. There are grounds for regarding the central reflex reactions recorded in these experiments as the result of the influence of mediators and anesthetics on the receptor structures of the superior cervical sympathetic ganglion. The results obtained also reveal new aspects of the mechanisms of general action of local anesthetics and mediators.

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