VASODILATOR EFFECTS IN THE LIMBS DUE TO STIMULATION OF THE SYMPATHETIC CHAIN

COMMUNICATION I. THE INFLUENCE OF THE FREQUENCY AND THE DURATION OF STIMULATION, AND OF THE CONDITION OF THE ANIMAL

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It may be taken as established that both vasodilator and vasoconstrictor nervous influences pass through the sympathetic system to the blood vessels. Most modern authors attribute vasoconstriction to the activity of special constrictor fibers which liberate noradrenalin at their endings, while dilatation is thought to be brought about by cholinergic elements of the sympathetic system [5, 7, 11]. It has been shown that according to the particular area affected, stimulation of different cell groups and fibers within the central nervous system may cause either a constriction or a dilatation of the vessels of skeletal muscle [9]. It is much harder to differentiate fibers of the two types in the sympathetic chain and in the peripheral nerve trunks. Despite careful studies, until now no nerve fibers whose stimulation could consistently produce dilatations of the vessels of a particular organ have been found within the sympathetic system; this effect occurs only erratically, and has been observed by certain authors under certain special conditions of stimulation. A. A. Ostroumov [1] was first to show that dilatation of the vessels of the limbs occurs when the strength or frequency of stimulation applied to the sciatic nerve is reduced. Subsequently it was established that reduction of the frequency of stimulation of the sympathetic chain [10] or increasing the duration of the stimulus [3] may also cause the vasoconstrictor effect to change over to one of vasodilatation [10].

It is thought that sympathetic vasodilators are present in the peripheral trunks, but that they are very few in number compared with the vasoconstrictor fibers. However, the idea that a particular response of an effector is associated with certain specific fibers responsible for the realization of the reaction is not the only possible view concerning the regulatory mechanism of the autonomic nervous system. M. G. Udel'nov [2], taking cardiac regulation as an example, has shown that cardiac output may be both potentialted and inhibited by the same nervous conductors. The nature of the response in any particular case is determined by the number of effector fibers excited, and by the frequency of stimulation of each one of them.

The object of the present investigation has been to determine to what extent the concept of lack of specificity of certain nerve fibers can be applied to the vasomotor system. If the different effects develop through stimuli which differ only in frequency and in the length of time for which they are applied, but which are identical in strength and duration of each stimulus [10], then it would seem to be difficult to explain the effects in terms of selective excitation of different kinds of nervous elements making up the stimulated nerve trunk. If the nature of the response is determined not by specific properties of the excited fibers, it then remains to explain the development of different responses. As a field for investigation we chose the vascular system of the hind limb.

METHOD

The experiments were carried out on cats under ether-urethane anesthesia. The sympathetic chain was stimulated at the 4-6th lumbar segments, and in most cases the sympathetic chain was left intact; control experiments were also carried out in which the peripheral end of the chain was stimulated after it had been divided at the 3-4th segments, and dissected out to the 5-6th lumbar segments. For this purpose we used implanted electrodes. As a stimulus we used a pulse generator which allowed the frequency to be varied from 0,1 to 250 cycles, the strength from

0 to 9 v, and the duration of the stimulus from 0 to 5 mseconds. According to Folkov [5], the maximum vasomotor response is attained at frequencies of 15-25 cycles. Because our observations confirmed these results, in our experiments the stimulus frequency did not exceed 20 cycles. The rate of blood flow indicating the condition of the vessels was recorded in the femoral vein by means of Gaddum's apparatus [6]. The rate is shown as the ordinate of the record, and the amplitude is directly proportional to the velocity of flow; in the absence of appreciable pressure changes a reduction in amplitude corresponds to a constriction, and an increase, to a dilatation of the vessels. During

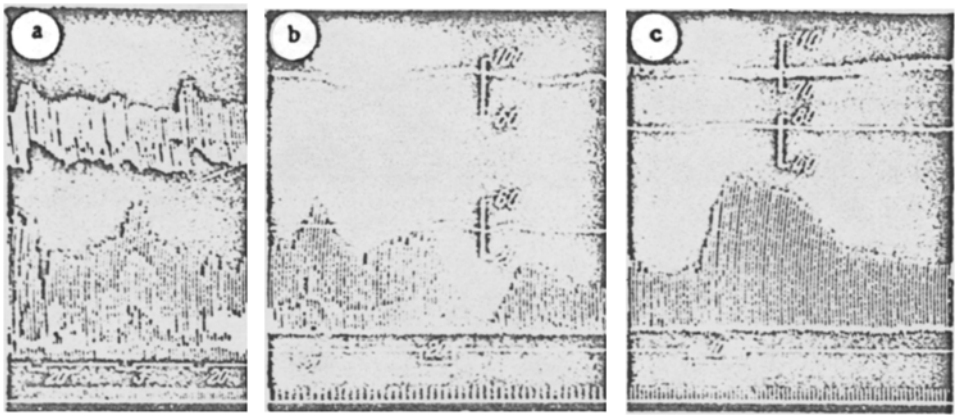

Fig. 1. Vasoconstrictor effects due to stimulation of the 5th lumbar segment of the sympathetic chain. a) Dilatation of the vessels as a result of stimulation at low frequency. Curves, from above downwards: arterial pressure (tonometer); rate of venous outflow; stimulus marker with number indicating frequency in cycles; time marker (3 seconds); b) dilatation of the vessels as a result of short-lasting stimulation at a constant frequency (experiment with crossed circulations). Curves, from above downwards; arterial pressure of donor; arterial pressure of recipient; rate of venous outflow from recipient limb; stimulus marker with frequency indicated in cycles; time marker (5 seconds); c) dilatation of the vessels in response to long-duration high-frequency stimulation (experiment with crossed circulation). Curves as in Fig. 1b) (Time marker – 3 seconds).

the experiment we recorded the arterial pressure in the carotid artery by means of a mercury manometer, and in some cases an elastic manometer was used. Two of the curves which are presented in this article were obtained with crossed circulation established by arranging for blood from the central end of the femoral artery of the donor to enter the femoral artery of the recipient. The amount of blood flowing from a vein of the perfused limb was recorded. The blood withdrawn was infused as a drip into the external jugular vein of the donor animal. An injection of heparin was given to prevent clotting.

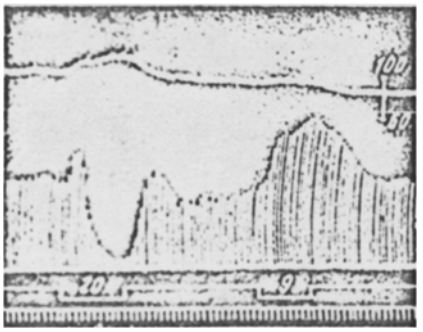

Fig. 2. Effect of frequency of stimulation and the nature of the vasomotor response. Stimulation applied to the 4th lumbar segment of the sympathetic chain in the donor animal. Curves, from above downwards: arterial pressure; rate of venous outflow; stimulus marker and figure indicating stimulus frequency in cycles; time marker (5 seconds).

RESULTS

In studying the vascular responses in the limb developing in response to stimulation of the sympathetic chain in the lumbar region, we were able to confirm the results of previous investigations. Figure 1a shows a curve from an experiment in which a 20-cycle stimulation caused a constriction of the vessels, while stimulation at 3 cycles caused a marked increase of the blood flow. A different form of the response is shown in Fig. 1b. Here the stimulus frequency was not changed. The different effects were obtained at a stimulus frequency of 20 cycles presented for different times – about 1 second and 25 seconds. The short-lasting stimulus caused a 50% increase of blood flow, while the prolonged stimulus caused a marked vasoconstriction. In the experiment whose results are shown in Fig. 1c, all the stimuli, independently of their frequency or duration, led to

a vasodilatation (the results shown are those obtained at a stimulus frequency of 10 cycles).

The experiments whose results are shown in Fig. 1b and c were carried out with the circulations crossed. The stimulation did not cause appreciable changes of arterial pressure; increase in the rate of blood flow could not have been due to this cause.

Under the usual conditions of an acute experiment, dilatation of the limb vessels is most easily observed in response to a short-lasting stimulation of the sympathetic chain (30-40% of the experiments). Other methods of stimulation cause vascular dilatation only exceptionally. Dilatation in response to all stimulus frequencies is very rarely observed. We were able to obtain such a result only in 3 of the 49 experiments. It is probably for this reason that in some communications it is claimed that the only effect of stimulation of the sympathetic chain is a constriction of the limb vessels [8].

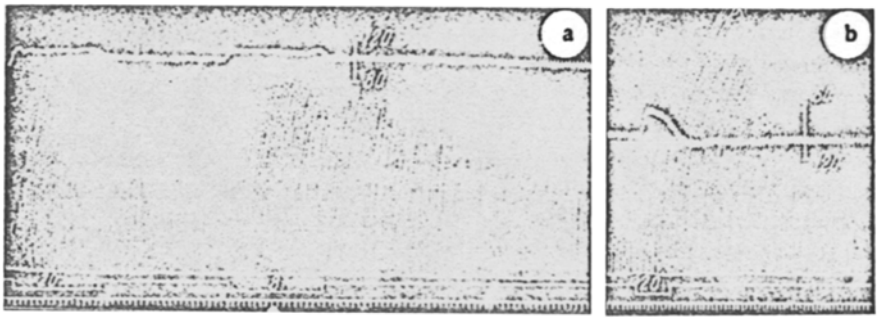

Fig. 3. Various forms of vasomotor response in experiments on the donor animal (stimulation of the 6th lumbar segment). Curves as in Fig. 2. (Time marker in Fig. 3a – 5 seconds; in Fig. 3b – 3 seconds).

Under such conditions, it is not possible to carry out a systematic investigation of the effects. It was important to find a method in which the vasodilator effects could be evoked very much oftener, and we succeeded in finding such a method. If the experiments are carried out with the circulations crossed (see above, under "Method"), then vasoconstrictor effects in the recipient are very seldom observed. However, if after several hours of work with crossed circulations the experiment is carried out only on the donor, then in this animal stimulation of the sympathetic chain will much more frequently evoke a vascular dilatation in the limbs. This type of reaction was observed in a donor dog in 9 out of 26 experiments, as compared with 3 out of 49 under usual experimental conditions. The vascular dilatation is very much more easily obtained by low frequency stimulation. The number of experiments on donor dogs in which no dilatation could be obtained did not exceed 20%. The transition from the constrictor to the dilator response was usually observed at frequencies which were higher than those used under normal conditions. For example, the curves in Fig. 2 show that stimulation at 20 cycles causes a biphasic effect in which the vasoconstrictor response preponderates, whereas at 9 cycles the effect is purely dilative.

In other experiments, the frequency "boundary" at which the transition from constrictor to dilator effects occurred varied at quite wide limits. Figure 3a illustrates another case, when both frequencies used (20 and 8 cycles) caused vascular dilatation, though at 8 cycles the effect was more intense, and lasted longer. In the experiment illustrated in Fig. 3b, all frequencies caused a dilatation of the vessels, and the maximal response occurred at 20 cycles. In our experience, use of frequencies above 20-25 cycles caused no further increase of the vasodilator effect.

Consequently, in normal animals, in the great majority of cases stimulation of the chain led to constriction of the vessels. In the donor animal, under the influence of some as yet unknown factors, the vasoconstrictor effect prevailed over the dilator response. Dilatation which was observed initially as a response to the very lowest stimulus frequencies became shifted during this transformation to occur at higher frequencies, until finally all stimuli evoked the dilatation.

As can be seen from the results, stimulation of the chain always causes an increase of pressure, which may be quite large. But, as has already been pointed out above, the increased blood flow can not be attributed to arterial pressure changes. For example, the curves of Fig. 3b show that the blood flow remains increased long after the pressure has fallen below the initial level.

We have therefore discovered definite experimental conditions under which stimulation of the sympathetic chain causes dilatation of the limb vessels.

SUMMARY

We showed that dilatation of the limb vessels in response to stimulation of the sympathetic chain occurred more frequently than in the usual experimental set-up if the animal used first served for several hours as a donor in a cross-circulation arrangement. In a considerable number of experiments with such animals, a vasodilator effect occurred in response to all frequencies of stimulation. When stimuli of varying frequency or duration provoked different effects, the dilatation of the vessels was attained only with stimuli of lower frequency and shorter duration than those which caused vasoconstriction.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.