CONDITIONS FOR THE APPEARANCE OF VASODILATOR EFFECTS IN THE LIMB VESSELS DURING STIMULATION OF THE SYMPATHETIC CHAIN

COMMUNICATION 2. VASOMOTOR EFFECTS OF STIMULATION OF THE SYMPATHETIC CHAIN UNDER HYPOTHERMIA

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Investigations of the circulation of the blood in hypothermia have mainly dealt with the study of the state of the heart muscle, the level of the arterial and venous pressure, and the changes in the vascular reflex responses to various afferent stimuli [1, 2, 8].

In the course of our researches into the mechanisms of the effect of vasomotor fibers, we came to the conclusion that a lowering of the body temperature of an animal causes a qualitative change in the reaction of the vessels to stimulation of the effector sympathetic fibers. The marked constriction of the vesssels usually observed in normal conditions is replaced by an equally marked dilatation.

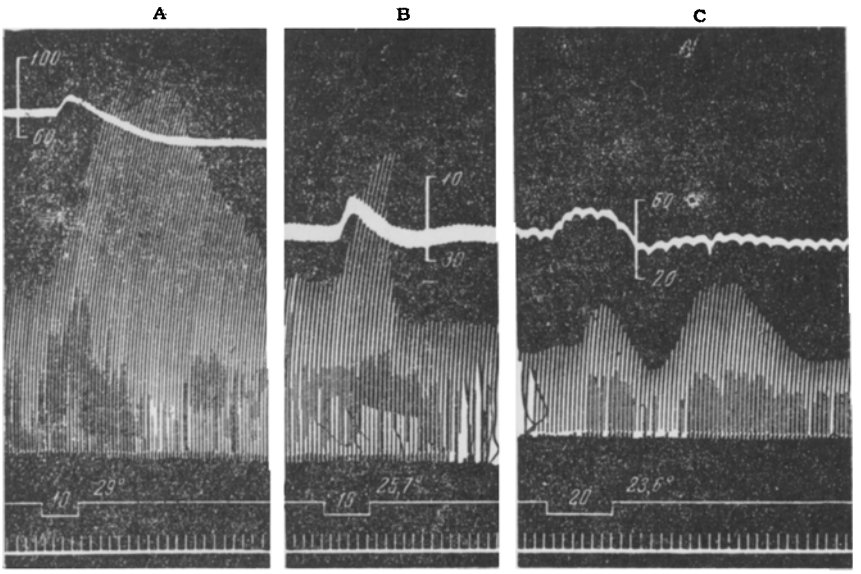

Fig. 1. Forms of vasomotor responses of the limb during stimulation of the 5th lumbar segment of the sympathetic chain in animals cooled to different temperatures (a, b, c). Significance of the curves (from above down): general blood pressure; rate of outflow of blood from the femoral vein; stimulus marker indicating frequency; time marker (5 seconds); the temperature recorded in the limb muscles is given above the stimulus marker.

We found no mention of these facts in the latest publications summarizing the results of study of the physiological functions in hypothermia [2, 8]. Nevertheless, much work was done on this subject as long ago as the end of last century [5, 7, 9]. Our findings are essentially merely the confirmation of facts known for a long time.

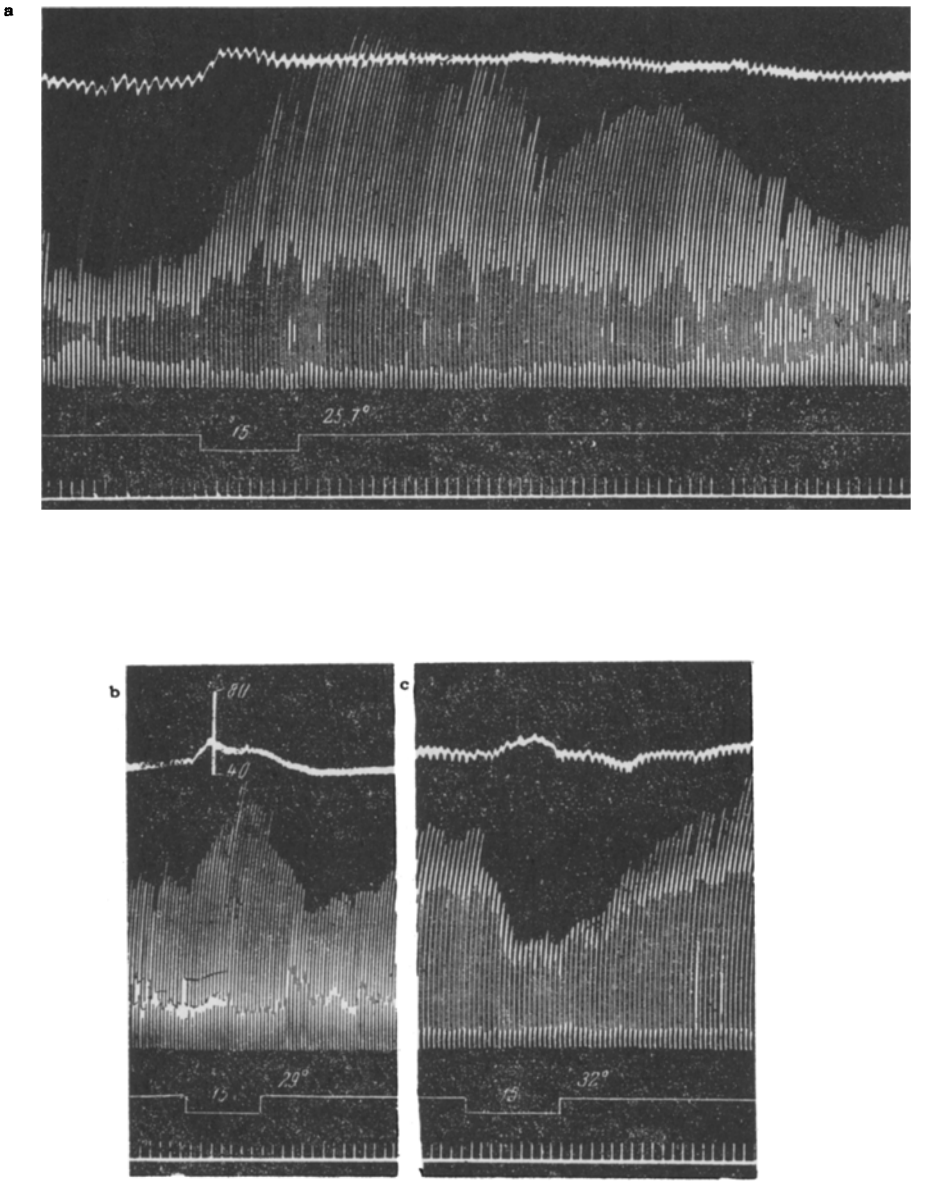

Fig. 2. Changes in the form of the vasomotor reaction of the limb observed in response to stimulation of the sympathetic chain in the lumbar region during the gradual elevation of the body temperature of a preliminarily cooled animal. Significance of the curves as in Fig. 1.

The interpretation of these facts from the modern point of view is of interest not only to the study of the physiology of hypothermia, but also in relation to the mechanism of the influence of the nervous system on the vessels.

EXPERIMENTAL METHOD

Experiments were conducted on cats under ether-urethane anesthesia. The velocity of the venous outflow was recorded by Gaddum's method [6], which permits the volume velocity of the blood flow to be expressed as a series

of ordinates, the height of which is directly proportional to the velocity of the blood flow. The ouflow was registered from the femoral vein, collecting blood mainly from the vessels of the limb muscles. The sympathetic chain was stimulated in the lumbar part at the level of the 4th-6th segments by means of a stimulator allowing the frequency, amplitude, and duration of the stimuli to be regulated independently. Hypothermia was produced by the method of "internal cooling," i.e., by cooling the blood [10]. The abdominal aorta was divided at the level of the middle lumbar segments, and blood from the central end was directed into a coil immersed in cold water. Blood from the coil was returned to the peripheral end of the divided aorta. The temperature was recorded in the muscles by an electric thermometer.

EXPERIMENTAL RESULTS

Dilatation of the limb vessels in response to stimulation of the sympathetic chain may be observed in ordinary experimental conditions only in rare cases. If the animal used for the experiment has previously served for a few hours as donor in a crossed circulation experiment, the vasodilator effects arise much more often and are much more marked. In some such experiments all frequencies and strengths of stimulation elicit only a vasodilator response [3]. What is responsible for the modification of the vascular reaction in an animal used as donor in a crossed circulation experiment? From an analysis of the experimental conditions it became clear that the blood passing through the recording apparatus and then into the body of the donor animal is cooled as a result of contact with the surrounding air.

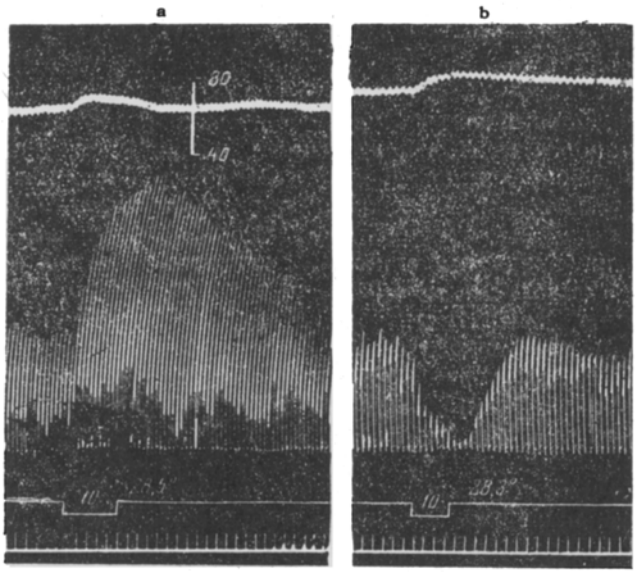

Fig. 3. The effect of atropine on the vasodilator effect obtained during stimulation of the sympathetic chain in the segment in a cooled animal. a) Before injection of atropine; b) after injection of atropine in a dose of 0.1 mg/kg body weight. Significance of the curves as in Fig. 1.

Measurements showed that at the end of an experiment lasting 1-3 hours, the donor's body temperature was always 2-4° lower than the recipient's, being 29-33°. Was this fall in body temperature resulting from the introduction of cooled blood the cause of the change in the reaction of the vessels of the donor animal to stimulation of effector fibers? Our experiments confirmed this suggestion.

The lowering of the body temperature by the method described above caused a change in the character of the response of the vessels to stimulation of the sympathetic fibers. In Fig. 1 we show the changes in the blood flow in the limb observed during stimulation of the sympathetic chain in a cooled animal. In all the cases cited the effect took the form of an increase in the velocity of the blood flow, varying in its intensity and duration. According to our observations, the most marked vasodilatation could be found when the body temperature fell to 28-30°, although at these temperatures a vasodilator response could be found in not more than 50% of the animals. The

rest gave the usual vasoconstrictor reaction. At 24-27° a vasodilator response was observed in most experimental animals, but its magnitude was diminished. At 17-20° all vasomotor responses disappeared. In some animals no vasodilator responses whatever could be observed—during gradual cooling the vasoconstrictor response gradually diminished until it disappeared completely (in 3 of 18 experiments). Factors such as extremely rapid cooling of the body (as observed when the temperature of the water in which the coil was immersed was not more than 5-8°) of the rapid repetition of the stimulation of the chain prevented the appearance of the vasodilator effects.

An increase in the body temperature led to restoration of the initial, i.e., the vasoconstrictor response. The curves are shown in Fig. 2, the first of which was obtained at a body temperature of 25.7°. Stimulation was accompanied in this case by dilatation of the vessels. At 32° the same stimulation caused a vasoconstrictor response.

The vasodilator effects observed in the cooled animal were abolished by atropine. In Fig. 3a, we illustrate the vasodilator effect obtained in an animal at a body temperature of 28.5°. After injection of atropine, stimulation was accompanied by constriction of vessels. We observed the same result in relation to the dilator effects taking place in the donor animals.

In consequence of the experimental conditions a gradual lowering of the body temperature and a change in the character of the vasomotor response to stimulation of the sympathetic chain thus took place in the donor animal. Cooling of the animal by a different method led to analogous changes in the vasomotor response. The similarity between these vasodilator reactions is also stressed by the fact that they were both abolished by atropine. These results give weighty support to the view that changes in body temperature are in fact responsible for the character of the vascular reaction to stimulation of the sympathetic chain.

We must point out, however, that there is a slight but essential difference between the experiments on the donor animals and on the cooled animals. In the first case a vasodilator vasomotor response took place when the body temperature had fallen only to 30-33°, but in the second a deeper degree of hypothermia was necessary to change the vasomotor reaction. This difference may have been due to a difference in the rate of fall of the temperature. It is also possible that some other, as yet unknown factors may influence the donor animal, facilitating the development of a vasodilator response.

The vasomotor effects described in this paper were obtained during stimulation of the intact sympathetic chain, in which both effector and afferent fibers were present. The question arises whether reflex influences play any part in the vasomotor effects we observed. We accordingly carried out a series of control experiments in which the vasomotor reactions were obtained by stimulation of the peripheral end of the sympathetic chain divided at the level of the 4th-5th segments and dissected over the course of the 1 or 2 segments below this level. It was shown that there was no significant difference in the character of the vasodilator response of the limb. Only the reaction of the general blood pressure to stimulation was modified. The rise of blood pressure observed during stimulation, and arising even when the limb vessels were dilated, was reflex in nature.

An attempt may be made to answer the question, which organs were responsible for the changes observed in the character of the vasomotor reaction. As we showed above, dilatation of the vessels may be observed in a cooled animal (donor) during stimulation of the peripheral end of the dissected and divided chain. Consequently, dilatation arises as a result of stimulation of the preganglionic sympathetic fibers. The change in the vasomotor reaction was evidently due to processes taking place either in the sympathetic ganglion or at the periphery—in the region of the neurovascular synapse or the smooth muscle of the vessel. In his studies of the sympathetic ganglion in hypothermic conditions, A. I. Shapovalov [4] showed that no changes take place in the transmission of excitation from the preganglionic to the postganglionic fibers at a body temperature of 25-26° if the frequency of stimulation does not exceed 15 cps, although frequencies of 20-25 cps begin to under transformation into a lower rhythm. Vasodilator effects may be observed, as we have seen, at higher temperatures than 26°. In the initial stages, moreover, dilatation of the vessels arises only during low frequencies of stimulation of the order of 3, 5, or 8 cps [3].

These facts suggest that the change in the character of the vasomotor reaction in hypothermia is not related to a disturbance of conduction in the sympathetic ganglion, but is due mainly to the influence of a lowered body temperature on the processes taking place at the periphery, i.e., in the smooth muscle of the vessel and in the region of the neurovascular synapse.

A fall in the animal's body temperature thus leads to essential changes in the reaction of the limb vessels to stimulation of the sympathetic effector fibers. Whereas in normal conditions vasoconstriction is observed in the overwhelming majority of cases, with even a slight fall in the body temperature (28-29°) a marked vasodilator res-

ponse is found in a considerable proportion of experiments. With a further lowering of the temperature this effect diminishes and it disappears completely at 17-20°. A leading part in the production of the vasodilator effect is evidently played by the influence of the lowered temperature on the neurovascular synapse and on the smooth muscle of the vessel.

SUMMARY

As shown, hypothermia leads to the change of the vascular reaction in the extremities in response to the stimulation of the sympathetic chain (its lumbar portion). In reducing the body temperature to 28-19° a considerable vasodilatation, instead of the usual vasoconstriction, was noted in a considerable number of experiments. This effect diminishes, with further temperature reduction, disappearing entirely at a temperature of 17-20°C. This leads to a conclusion that the changes in the character of the vasomotor response are caused by the effects produced by reduced temperature on the smooth muscle on the vessels and on the neurovascular synapsis, not on the excitation transmission in the sympathetic ganglion.

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