THE REFLEX CONTROL OF VASCULAR TONE DURING HYPOTHERMIA

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 50, No. 9, pp. 65-69, September, 1960

Original article submitted August 31, 1959

With the ever-increasing use of hypothermia in surgical practice, certain physiological indices require evaluation at low body temperatures. From this point of view the study of the reflex control of the blood pressure in hypothermia is of undoubted interest. In the literature, there are many reports of investigations of the state of the cardiovascular system during general hypothermia. Particular attention has been paid to the study of the cardiac function in hypothermia. The existing information on the control of the blood vessels in these conditions is, however, of a very limited character, although the subject is of considerable interest.

In carrying out this research we had two aims in view: to elucidate firstly, the general pattern of the disturbances of reflex control of the vascular tone in hypothermia and, secondly, some aspects of the mechanism of these disturbances.

METHOD

The first series of experiments was performed on dogs, cats, and rabbits. The animals were subjected to general cooling by being placed in a metal bath with a double bottom, which was cooled with ice or snow. The anesthetized animal was fixed on its back to the cold bottom of the bath, and ice-bags were applied to the anterior surface of its trunk. The rectal temperature fell gradually and reached 26° after 1-1½ hours. With further cooling, the temperature fell rapidly, to reach 20-19° after 20-25 minutes. Animals whose degree of hypothermia was so deep usually died from respiratory arrest before the conclusion of the experiment. For this reason, in the majority of experiments the animals were taken from the bath at 26-24° and kept at room temperature. Under these conditions the rectal temperature remained at this low level for 2-3 hours.

In some experiments hypothermia was induced by the method of extracorporeal cooling of the blood after preliminary heparinization. The femoral artery and vein were connected through a system of tubes and coils immersed in cold (4-5°) water. By this method the animals could be brought more rapidly into a state of hypothermia, and by immersion of the coil in warm (40°) water, the initial body temperature could be expeditiously restored.

The method of study of the reflex regulation of the vascular tone was as follows: In the anesthetized animal the sciatic and vagus nerves were dissected and placed on a ligature. In rabbits and, when possible, in cats, the aortic nerve was also dissected. A cannula for recording the blood pressure was introduced into the right carotid artery. Respiration was recorded from the trachea. The central ends of the nerves were placed on platinum electrodes and stimulated with rectangular impulses of current at a frequency of 50 imp/sec, the duration of each impulse being 10 msec and the voltage from 1 to 7v. The interoceptors of the urinary bladder were stimulated by increasing the pressure therein to 60-70 mm Hg. The receptors of the lungs and respiratory tract were stimulated by increasing the pressure in the closed system of the air passages to 100-120 mm water. The carotid sinus pressor reflex was evoked by clamping the left common carotid artery, and acute asphyxia by closure of the tracheal cannula. The vascular reflexes in response to stimulation of these sensory nerves and interoceptive fields were investigated before cooling, during the development of hypothermia and, in some experiments, after the animal had been warmed to its original temperature.

RESULTS

In a state of hypothermia, in addition to a considerable fall in the level of the arterial pressure and an increase in the pulse pressure, a marked weakening was observed in the reflex vascular reactions in response to stimulation of the central ends of the various sensory

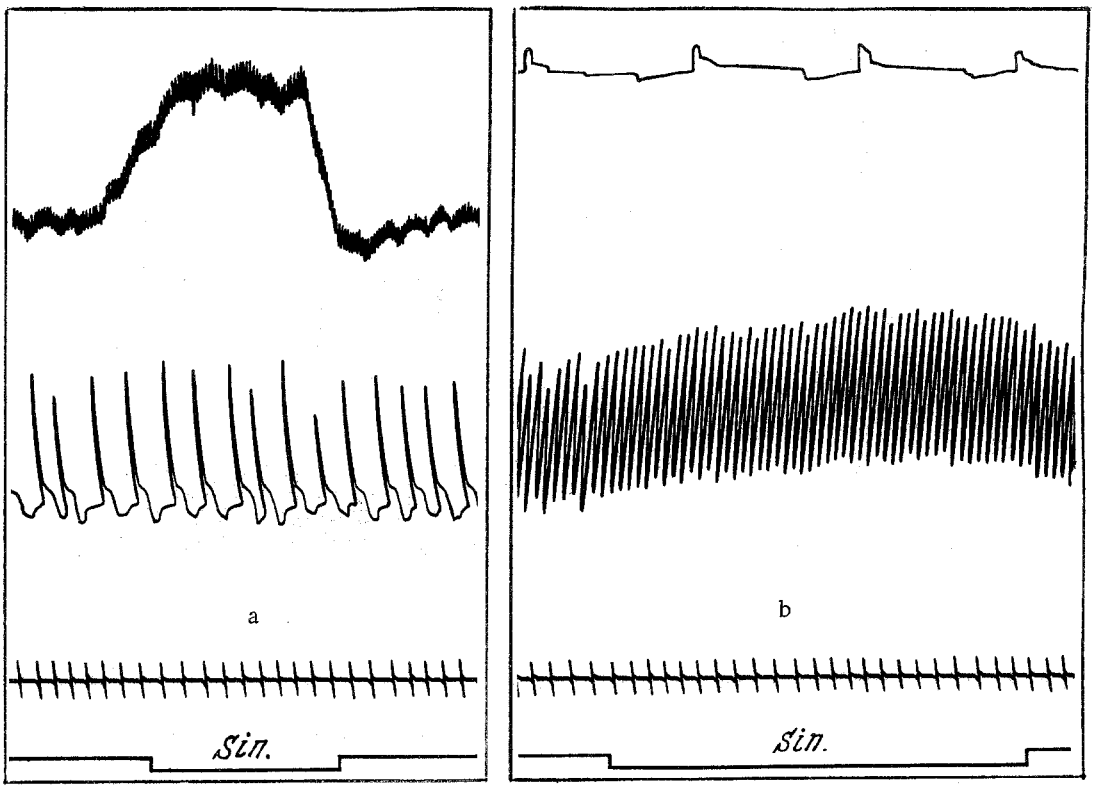

Fig. 1. Pressor reflex to a lowering of the pressure in the carotid sinus before (a) and during (b) the development of general hypothermia. Significance of the curves (from above down): a) blood pressure, respiration, time marker, stimulation marker; b) respiration, blood pressure, time marker, stimulation marker.

nerves and interoceptive zones. These findings are illustrated in Figs. 1 and 2.

It must be pointed out that the depressor reflexes were weakened more rapidly and to a greater degree than the pressor reflexes. This can be understood in the light of the views expressed by I. A. Arshavskii [1], B. D. Kravchinskii [2], V. N. Chernigovskii [7] and others, that the depressor mechanisms are phylogenetically younger than the pressor, and are consequently more susceptible to injury. In some experiments the depressor reflexes in response to stimulation of the central end of the vagus and aortic nerves were distorted with the background of hypothermia. The most resistant of the depressor reflexes was the one which occurred in response to inflation of the lungs, although this, too, was considerably diminished during hypothermia. Further cooling of the animal to 20° led, as a rule, to the disappearance of all the vascular reflexes.

In the animals in a state of hypothermia, the vascular reaction to acute asphyxia was also weaker than normal, and developed only after a prolonged latent period.

A decrease in the various vascular reflexes during hypothermia has been described by many authors. T. V. Popova [3, 4], for instance, observed a weakening of the interoceptive reflexes from the stomach and urinary bladder during general hypothermia (26°); Dubecz, Kertai, Kokas, and Ludany (cited by [8]), and also K. M. Mokhin and B. A. Saakov [5] described a considerable weakening of the pressor reflexes from the receptors of the carotid sinus; B. A. Saakov [6] observed a diminution of the vascular reflexes during hypothermia resulting from stimulation of the vagus and superior laryngeal nerves and also of the chemo- and mechanoreceptors of the carotid sinus.

The results obtained by these authors, like our own experimental findings described above, demonstrate that during hypothermia the reactivity of the vascular system is significantly depressed. This regularly applies during stimulation of different afferent links of the vascular reflexes.

Most authors who have studied the vascular reactions during hypothermia have, unfortunately, limited themselves to a plain statement of facts, without attempting to discover the mechanisms on which these changes are based. The reports in the literature of the role of the receptors, as the initial link in the reflex arc, in the changes in vascular control observed during hypothermia, do not give any clear idea of the actual state of affairs. K. M. Mokhin and B. A. Saakov [5], and B. A. Saakov

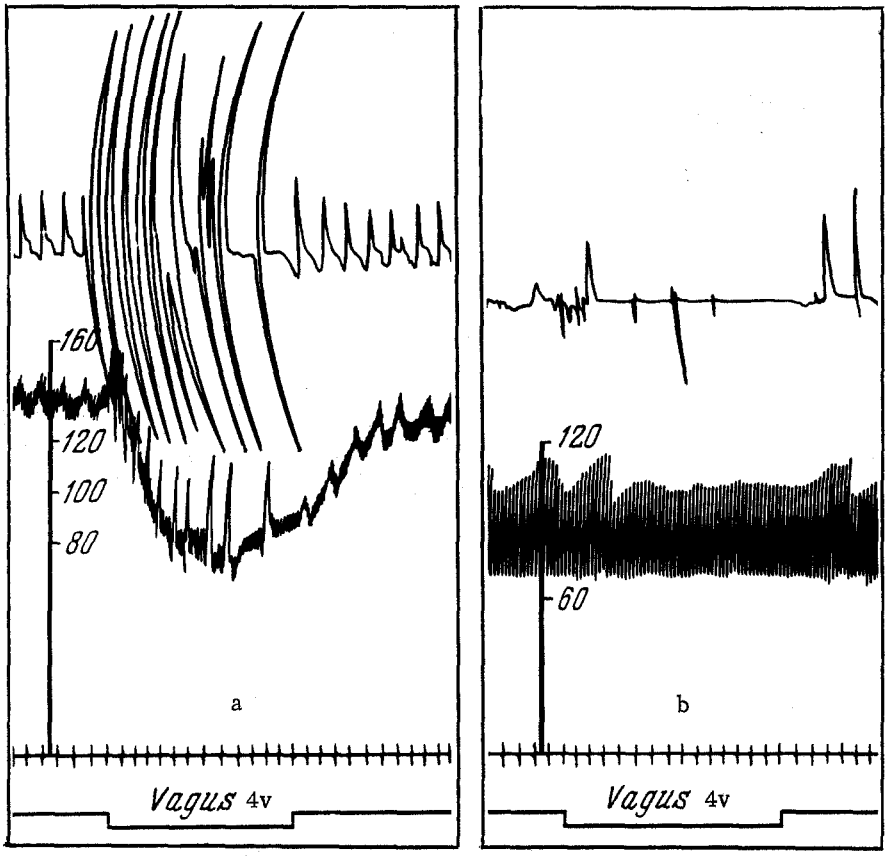

Fig. 2. Stimulation of the central end of the vagus nerve before (a) and during (b) the development of hypothermia. Significance of the curves as in Fig. 1.

[6], for instance, noted a decrease in the reflexes from the carotid sinus during hypothermia, and ascribed these changes to a lowering of the excitation of the carotid sinus receptors, although they did not conduct any direct investigations of the level of excitation of the receptor apparatus. T. V. Popova examined the effect of local cooling of the stomach and urinary bladder on the interoceptive reflexes from these organs by irrigating the interior of these organs with cold (4°) solution, and in these conditions observed weakening of the interoceptive reflexes, although to a less pronounced degree than during general hypothermia (26°). No precise details were obtained of the temperature of the organ under study, although this was a decisive factor.

More definite results were obtained in work by Malmejac and Neverre [8]. These authors perfused the isolated carotid sinus with cooled blood and observed that the reflexes from the pressure receptors were preserved during cooling of the sinus to 29-20°. Tournade and Dubreuil [9], however, who perfused the carotid sinus with Ringer's solution at different temperatures, observed a decrease or the complete absence of the depressor reflexes from the cooled sinus at a perfusate temperature of 20°.

In order to elucidate the role of the receptor link in these disturbances of control of vascular tone which are observed during hypothermia, we conducted a series of experiments on the carotid sinus, isolated by Moiseev's method, which was perfused with Ringer's solution at a given temperature. The temperature of the solution entering the common carotid artery could be altered by means of a coil, immersed in either warm (39°) or cold (26-19°) water. The temperature of the fluid flowing from the carotid sinus was continuously measured by means of a mercury thermometer. The chemoreceptors of the carotid sinus were stimulated by means of injection of solutions of adrenalin, nicotine, and acetylcholine of suitable concentration into the perfusion fluid, and the pressure receptors were stimulated by raising the pressure of the Ringer's solution in the sinus to 180 mm Hg. The initial magnitude of the vascular reflexes arising from the various forms of stimulation of the isolated carotid sinus were recorded during perfusion with warm solution. When the perfusion fluid was changed to Ringer's solution at a temperature of 26-19°, i.e., the cooled solution, the blood pressure measured in the central segment of the carotid artery rose by 10-20 mm Hg and was maintained steadily at this level throughout

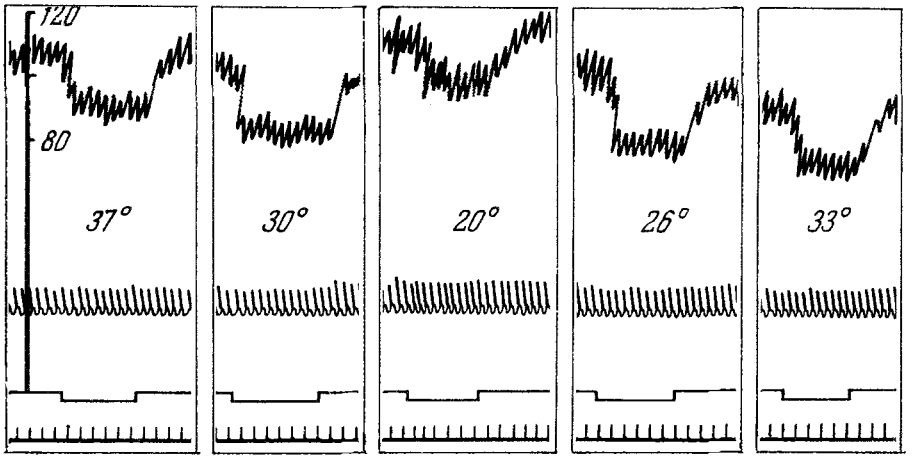

Fig. 3. Increase of pressure in the isolated carotid sinus before and during perfusion with cold solution. Significance of the curves (from above down): arterial pressure, respiration, stimulation marker, time marker. The temperature of the fluid flowing out of the carotid sinus is indicated on the kymograms.

the whole period of cooling of the carotid sinus. The carotid sinus reflexes were recorded 5-15 minutes after the beginning of perfusion with the cold solution.

In some experiments the central end of the carotid artery was connected through the coil to the isolated carotid sinus, and the outflowing blood entered the jugular vein. The blood passing through the coil was cooled to 26-20°. In these conditions we studied the pressor reflex while the pressure within the carotid sinus was lowered before and during the cooling of the sinus.

The experiments on the cooled, isolated carotid showed that the receptors of the sinus suffered no decrease in their sensitivity to the various chemical stimuli and to changes in the intravascular pressure when cooled to 26-20°. On the contrary, within this range of temperature, the level of excitation of the receptors of the carotid sinus may even be higher than normal (Fig. 3). The changes in the interoceptive vascular reflexes during hypothermia are, therefore, not the result of a fall in the excitability of the receptors.

SUMMARY

The vascular reflexes were studied in dogs, cats, and rabbits during stimulation of the receptors of carotid sinus, lungs, and urinary bladder; the reflexes were also investigated during stimulation of the sensory nerves (vagus, aortic, sciatic). A marked reduction of all vascular reflexes was noted during hypothermia; they disappeared almost completely when the body temperature dropped below 20° C.

Depressor reflexes were subjected to more rapid and profound depression than pressor. To investigate the role of the receptor link in the changes mentioned, experiments were carried out with the local application of cold upon the carotid sinus receptors. It was found that when cooled to a temperature of 20-26° C the carotid sinus receptors showed no reduction of their sensitivity either to various chemical stimulants or to changes in the intravascular pressure. On the contrary, within this temperature range the excitability of the receptor formations was even higher than normal.

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