REFLEX REGULATION OF VASCULAR TONE WHEN THE BRAIN IS ISOLATED AND COOLED

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 53, No. 1, pp. 7-11, January, 1962
Original article received March 2, 1961

In the extensive literature dealing with regulation of vascular tone during generalized hypothermia, the opinion is held, and supported by factual evidence, that when the body temperature is reduced to 26 - 23°, there is a marked suppression of reflex regulation of the vascular zone, and when the temperature falls to about 20°, as a rule no such reflexes can be evoked. We have investigated this problem, and have studied vascular responses to stimulation of receptors of the lungs, urinary bladder, and carotid sinus, as well as to stimulation of the central ends of the sciatic, vagus, and depressor nerves.

Most authors who have worked on the problem of hypothermia consider that disturbance to any particular bodily function during cooling results from the indirect suppressive influence of cold on the central nervous system.

Comparatively few direct experiments have been done on the isolated action of cold on the central nervous system. We must note however the work of P. M. Starkov and his pupils [2, 3, and others], in which the influence on respiration and arterial pressure was demonstrated by direct cooling of the autonomic centers. Perfusion of the cerebral ventricles with a cold solution showed that when the temperature of the effluent fluid was 19°, there was always a reversible arrest of circulation, and the arterial pressure suffered consistent alterations. Unfortunately, they made no study of the reflex excitability of the respiratory and vasomotor centers under these conditions, and even the temperature attained by the brain tissue was not known.

Interesting work on the influence of hypothermia on the responses of the central nervous system was carried out by Suda, Koizumi, and Brooks [7]. They used cats, and cooled the brain and spinal cord by cold blood introduced into the abdominal aorta and carotid arteries, and by cold mineral oil covering the exposed spinal cord. At a brain temperature of 35-25° a hyper-reactive phase developed, and the amplitude of the electroencephalographic waves increased as did also the amplitude of the action potentials from the cerebral and cerebellar cortices, and the number of neurones in the spinal cord responding to stimulation of the peripheral nerves increased, etc. Only at lower temperatures was excitability decreased.

The researches of Malmejac, Neverre, Montero and Fredenuchchi [6], in which the brain was isolated humorally and cooled, undoubtedly deserve serious attention. They studied the alteration of the pressor response in the trunk, where normal temperature was maintained, when the pressure in the cerebral vessels was lowered at various stages of cooling. It was shown that in hypothermia of the brain, the pressor response is weakened, and disappears at 19 - 20°. The change is the direct result of cooling the nerve centers, as is shown by the very low sensitivity of the receptors of the isolated carotid sinus to cooling. The possibility of a cold block of the conducting pathways within the brain with this method was excluded, because as other workers have shown, partial block of these pathways occurs only at a temperature of 8°.

On the other hand, N. V. Semenov [5] showed that when the brain is cooled to 25°, the reflex changes of arterial pressure in response to stimulation of the vascular reflexogenous zones are maintained.

Our experiments were carried out by cooling the brain, which was completely isolated from any vascular connection with the head, and was perfused by blood cooled to a known temperature. The body temperature remained normal.

METHOD

It is recognized that the main difficulty in isolating the head is in stopping the flow to it through the spinal arteries and the flow along the venous sinuses lying within the vertebral canal. S. I. Baluev [1] described a successful method of overcoming this difficulty, and we used it in our experiments, as follows. At the rostral end of one of the vertebral arteries, and at a depth of 6 - 8 cm, a fine steel wire carrying at its end a compact plug of cotton wool was introduced so as to plug the opening of the artery. Then a small amount of AKR-7 plastic diluted in acetone was injected from a syringe into the same end of the artery; the solution penetrated the anastomoses into the spinal arteries where it set, thus blocking them. When the cotton wool is removed from the vertebral artery, all the excess plastic remaining within the vessel is removed, and the artery remains available for the next perfusion. Venous flow along the vertebral sinuses is stopped by a bilateral injection of plastic into the rostral ends of the ligatured vertebral veins. To facilitate access to the vertebral arteries and veins, all the anterior muscles of the neck are divided between ligatures. Blood flow along the posterior and lateral muscles of the neck is arrested by pressure from a clamp introduced beneath the carotid arteries, jugular veins, and vagal and sympathetic trunks, which had been dissected out.

The rostral ends of the carotid and vertebral arteries of dog A were connected by a system of tubes and spiral coils with the vertebral arteries of the donor B. Venous flow from the jugular veins of dog A into the jugular vein of dog B was maintained by a pump having input and output valves. The temperature of the inflowing and outflowing blood was measured by mercury thermometers in the tubes. Brain temperature was measured by a thermocouple introduced into the substance of the brain through a trepanned opening. To prevent clotting of the blood, both dogs received an injection of heparin. The head was cooled by placing the spiral in water of the appropriate temperature. To ensure an adequate supply of blood to the head of dog A, the donor dog was selected to have the greater weight.

A diagram of the experiment showing perfusion of a head humorally isolated from the trunk is shown in Fig. 1.

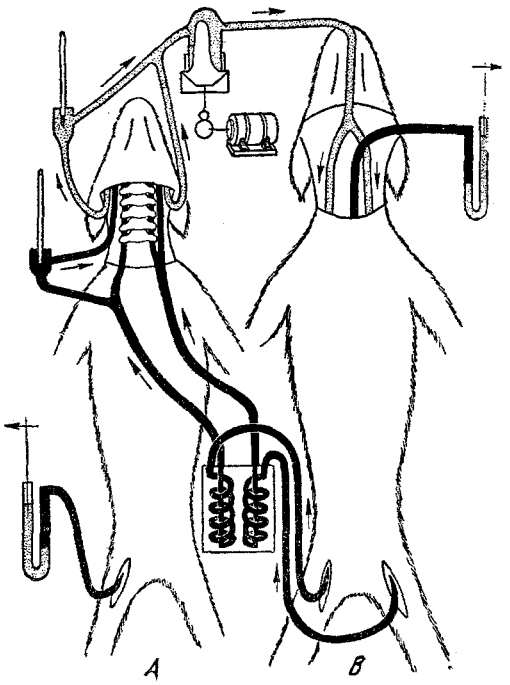

Fig. 1. Diagram showing perfusion of a humorally isolated head. Explanation in text.

In some of the experiments, instead of a donor dog, we used an "autojector" with artificial lungs.

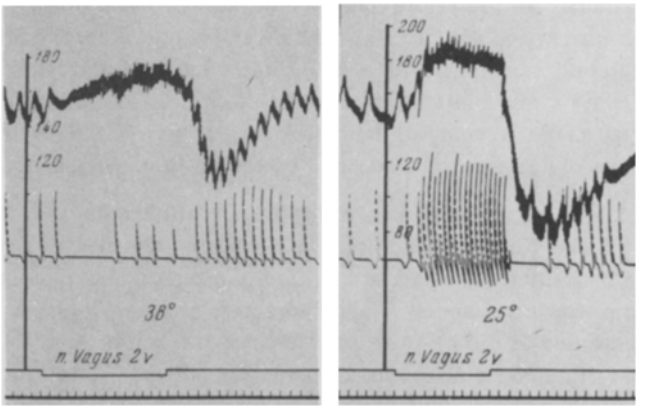

Fig. 2. Vascular response to stimulation of the central end of the vagus; on the left, before, and on the right, after cooling the brain to 25°. Perfusing the head with cooled blood was carried out by means of an "autojector". Curves, from above downwards: arterial pressure; respiration; stimulus marker; time marker.

Studies were made before and after cooling the head of the vascular responses to stimulation of the central ends of the vagus and of the sciatic nerves; also the effect of changing the perfusion pressure in the cerebral vessels was noted and measurements were made of changes in arterial pressure in the trunk vessels in response to the injection of adrenalin or acetylcholine into the head or trunk.

RESULTS

Experiments in which the brain was cooled to 26 - 24° while the normal body temperature was maintained established that: a) vascular reflexes involving cerebral centers (evoked by stimulation of the central end of the vagus nerve) are not depressed, but, on the contrary, in some of the experiments were somewhat enhanced (Fig. 2);

b) vascular reflexes involving cerebral and spinal centers (evoked by stimulation of the sciatic nerve) were increased above normal; c) reflex responses of the vessels of the trunk to change in the perfusion pressure of the cerebral vessels remained normal (Fig. 3); d) the direct sensitivity of the brain to humoral stimuli (adrenalin, acetylcholine) remained normal, or was increased (Fig. 4); e) the action of humoral stimuli on the trunk vessels was also better shown than normally.

Only when the brain temperature fell to 20° or below was there any suppression of vascular reflexes.

These facts indicate that the suppression of vascular reflexes observed when the whole body is cooled to 26 - 24° is not the direct result of the action of cold on the central nervous system.

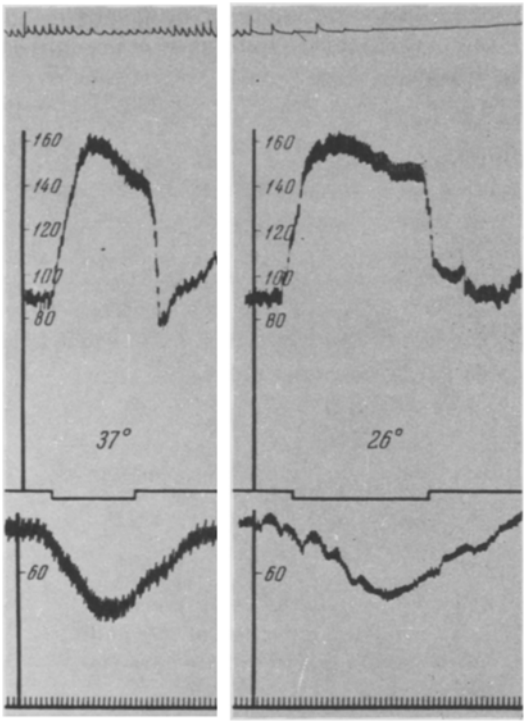

Fig. 3. Response of the vessels of the trunk to increased pressure in the cerebral vessels; animal perfused with its own blood by means of an autojector; on the left, before, and on the right, during cooling of the brain to 26°. Curves, from above downwards: respiration; perfusion pressure in cerebral vessels; stimulus marker; pressure in the femoral artery; time marker.

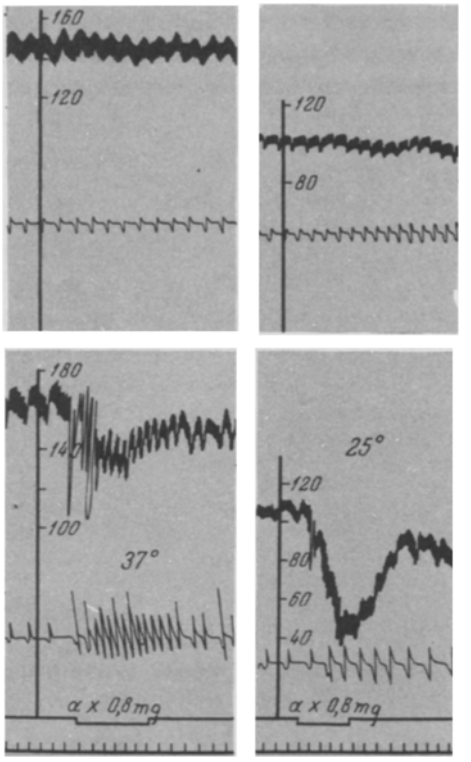

Fig. 4. Change of arterial pressure induced by the injection of acetylcholine; on the left – before, and on the right – after cooling the brain to 25°. Curves, from above downwards: arterial pressure of donor; respiration of donor; arterial pressure in femoral artery of experimental dog; its respiration; stimulus marker; time marker.

At the beginning of the article we pointed out that in studying reflex regulation of circulation in hypothermia, a large number of investigators have found a considerable depression of various vascular reflexes. This effect is due to a suppression of the central nervous mechanisms regulating vascular tone. Also, the isolated cooling of the brain, and therefore of the vasomotor centers, does not cause any depression of the vascular reflexes. We may therefore conclude that cold by itself, of course within certain limits, does not exert any direct suppressive influence on the vasomotor centers.

Suppression of the central nervous mechanisms regulating vascular tone, which always occurs during sufficiently deep generalized hypothermia, is probably the result of a reflex influence of the numerous interoceptors of the cooled tissues.

SUMMARY

When a dog's head was isolated humorally and cooled to 24 - 26° while the rest of the body remained at normal temperature, no significant depression of control over vascular tone was observed.

We showed that the vascular reflexes elicited by stimulating the central end of the vagus nerve were normal, or even somewhat augmented. The reflex reactions of the vessels of the trunk remained normal when the perfusion pressure in the vessels to the head was changed; the direct sensitivity of the brain centers to the action of the humoral stimulants adrenalin and acetylcholine either remained normal or was somewhat increased; depression of the vascular reflexes was observed only when the brain temperature was reduced to 20° or less.

These facts indicate that within certain limits, cold does not exert any direct depressant effect on the nerve centers controlling vascular tone. Depression of vasomotor centers, which always occurs in general hypothermia, is evidently caused by the numerous interoceptors of the cooled body tissues.

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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.
