INDUCTION OF HYPOTHERMIA BY DIRECT COOLING OF THE BRAIN THROUGH ITS EXTERNAL COVERINGS

N. V. Klykov

From the Chair of Normal Physiology (Director: Prof. P. M. Starkov), Kuban Medical Institute

(Received October 23, 1956. Presented by N. N. Gorev, Member AMS USSR)

The changes observed in the organism as a result of its general cooling are in the first place due to progressive inhibition of the central nervous system. The result of this inhibition is to produce step-wise abolition of its functions, beginning with the cerebral cortex. Conditioned reflex activity is abolished in dogs when the body temperature falls to 28-30° [4]. Changes take place in the electrical activity of the cerebral cortex, which becomes weaker as the temperature falls, finally ceasing altogether [10, 12, 3].

Disturbance of function of the between-brain and the mid-brain takes place much later [10], while the functions of the medulla oblongata and the spinal cord persist to lower temperatures, and are the last to be abolished [1, 4].

Procurement of profound inhibition of the central nervous system by means of generalized lowering of body temperature is now widely applied clinically, in particular in connection with heart surgery [12, 8, and others]. The induction of generalized hypothermia, especially in its more extreme forms, is by no means a safe or a simple undertaking, either in the human or in animals. One of its most dangerous complications in surgical practice is the development of ventricular fibrillation, in particular when the heart has been excluded from the circulation. The frequency of incidence of fibrillation is in direct proportion to the degree of cooling of the organism [8, 9, 15]. This fibrillation greatly limits the possibilities of applying hypothermia. It is of importance to find ways and means of preventing its onset.

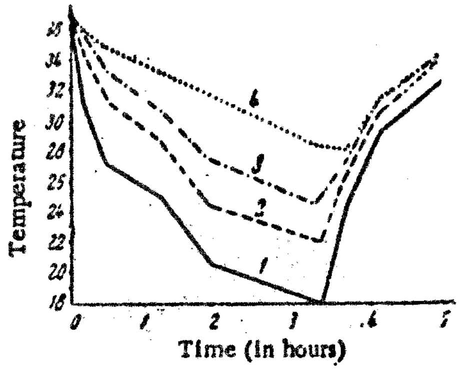
The useful effect of hypothermia under conditions of exclusion of the action of the heart is that it protects the central nervous system, and in particular the cerebral cortex, from the harmful effect of the resulting anoxia, since the tolerance of the brain to oxygen lack is much higher in the hypothermic state [6, 2]. It follows from this that the most important aspect of hypothermia is the lowering of the temperature of the brain, and in particular of its higher levels. This points to the possibility of inducing hypothermia by cooling the head alone, leaving the rest of the body at a relatively high temperature; since this includes the heart, it may fully prevent its fibrillation. The cooling of the brain through the cranium is quite feasible, since of all tissues bone is the best conductor of heat. It should in this connexion be mentioned that Nikitinov [7] proposed the application of cold to the head for the treatment of certain brain conditions, as far back as 1885.

Attempts at clinical applications of cold to the head have been described in the literature. Thus Fay and Smith [13], who treated cancerous disease by hypothermia, applied ice-packs not only to various parts of the body of the patient, but also to the head. Fay [14], in the treatment of headaches of varied etiology, used a special helmet placed on the head, with a stream of cold water running through it.

The present paper describes a study of the induction of hypothermia by cooling the brain alone, through its external coverings, and of the temperature profiles achieved at different levels.

EXPERIMENTAL METHODS

In all, we performed 17 experiments on cats. Cooling was effected by means of a small cooling blanket, in which the head of the animal was wrapped. The hair had first been thoroughly removed from the head. Water at 3-5° was circulated through the blanket. Temperature readings were recorded simultaneously from two or three levels of the brain, using a copper-constantan thermocouple, the insulated function of which was enclosed in a hollow needle with a closed end. At the same time rectal temperature was measured by means of a mercury thermometer inserted to a depth of 8 cm.



Rate of fall and rise of temperature at different levels of the brain and in the rectum during external cooling of the head, with subsequent warming of the organism. 1) Upper layer; 2) middle layer; 3) deep layer; 4) rectum. Cat, body weight 2.8 kg. Experiment of the 4th May 1956.

In some of the experiments we did not insert the thermocouple needles, in order to avoid injury to the brain, but judged the brain temperature from that of the blood returning from the brain in the jugular vein. For this purpose we inserted a very thin and smooth thermocouple into the vein, against the direction of the current of blood. Control experiments showed that the temperature of the blood was very close to that of the brain.

Arterial pressure was recorded from the carotid artery by means of a mercury manometer, and respiration by means of a Marey capsule, connected through a four-way tube to the trachea. Ether anesthesia was applied.

Restoration of brain temperature was achieved by warming the whole body with an electric heater until the rectal temperature reached 33-34°, with a short period of heating of the head at the beginning of the recovery period.

EXPERIMENTAL RESULTS

Different temperatures were recorded from different levels of the brain (upper, middle, deep) during the cooling process. As is evident from the Figure, the temperature fell fastest in the outer layer, and more slowly in the middle one (subcortical region). The temperatures of the basilar regions of the brain differed considerably from the two preceding regions. The temperature of the rest of the body fell to some extent, but remained high, relative to the brain. At the end of the period of cooling, the brain temperatures (means of 10 determinations) were: upper layer (cortex) about 18°, middle layer (subcortical) 21.2°, while the rectal temperature was 29°. The temperature of the base of the brain (mean of 4 experiments) was 24.7°.

TABLE 1

Changes in Arterial Pressure, Heart Rate, and Respiratory Rate During External Cooling of the Brain (temperatures relate to the mid-brain). Means of 9 Experiments

Brain temperature / Function	Cooling phase					Rewarming phase		
	37°	35°	30°	25°	20°	25°	30°	33°
Arterial pressure, mm Hg	137	140	114	101	93	106	122	134
Heart rate, beats per minute	176	172	160	134	110	114	130	158
Respirations per minute	27	24	23	19	14	19	18	23

Thus the characteristic feature of our experiments was the considerable temperature difference between the brain, and particularly of its upper layers, and the rest of the body.

The same regularity was evident when jugular vein temperatures were measured; rectal temperature remained at a high level, as compared with jugular vein temperature. Thus when the rectal temperature was 36.5° (mean of 8 measurements), and the jugular vein temperature was 35.8°, before cooling, the corresponding temperatures at the end of the cooling process were 30.9° and 21.8°. The length of the cooling process for these experiments was 90 minutes, on the average. Return to normal body temperature lasted for 94 minutes.

Cooling of the head alone was associated with circulatory and respiratory changes. As the temperature fell in the brain, there was a gradual fall in arterial pressure, which, however, rose slightly at the beginning of the cooling process, when the brain temperature was 35° (Table 1). The mean fall in pressure when mid-brain temperature was 20° was to 67.8% of the initial value (mean of 9 experiments). The heart rate also fell gradually, to 62.5% of the initial value when mid-brain temperature was 20°. No disturbances of heart rhythm were observed during the cooling process.

The respiratory rate had fallen to about half the initial value when the mid-brain temperature had fallen to 20°, amounting on the average to 51.8%.

Similar effects were found in the experiments in which jugular vein temperatures were measured (Table 2). Slight shivering was noted during the cooling process.

TABLE 2

Changes in Arterial Pressure, Heart Rate, and Respiratory Rate During Cooling of the Brain (temperatures measured in the jugular vein). Means of 8 Experiments

Jugular vein temperature / Function	Cooling phase					Rewarming phase		
	36°	34°	30°	25°	22°	30°	32.5°	35°
Arterial pressure, mm Hg	145	138	120	104	86	110	121	129
Heart rate, beats per minute	202	182	168	138	120	149	174	200
Respirations per minute	20	18	16	13	13	16	20	22

The rise in brain temperature after cooling was accompanied by restoration of normal circulatory and respiratory functions. As is evident from Table 1, arterial pressure rose practically to normal (98%, on the average) when brain temperature had risen to 33°, and in three experiments it was fully restored.

The heart rate increased rapidly, regaining its initial value when jugular vein temperature had risen to 35° (Table 2). Rise in respiratory rate and amplitude also accompanied rise in brain temperature.

It thus appears that the respiratory and circulatory indices studied by us were rapidly and almost completely restored to normal after profound cooling of the brain.

The skin incisions were stitched up after the temperature had returned to normal. The animals were given penicillin for a few days after the experiments, in order to prevent infection.

The cats were languid and inactive after the experiments, and lay down in normal attitudes; their sensitivity to pain was lowered, but they reacted to sound and light. Their condition was considerably improved by the next day, and they fed spontaneously. More prolonged observation of the animals did not reveal any deviations from the normal.

A hypothermic state can therefore be achieved by cooling the brain alone, through its external coverings. This procedure leads to a fall in both rectal and brain temperatures, but, in view of the direct application of cold to the head, brain temperature falls faster and lower than rectal. We found similar effects [5] when the brain was cooled by extra-corporeal cooling of carotid artery blood. Using this procedure, we reduced brain temperature to 20°, when rectal temperature was about 30°. When the body as a whole is cooled, these temperatures are practically identical [11].

Cooling of the brain is achieved in our experiments by direct loss of heat from the interior of the brain to the cranium and scalp. As a result, the superficial parts of the brain, in the first place its cortex, lose heat faster than the underlying parts, so that its temperatures falls faster, and to a lower value, than in the lower levels. Such a differential gradient of temperatures in the brain and in the whole organism may be very convenient. More intense cooling of the cortical regions may lead to more profound inhibition of function than in the subcortical regions and the brain stem. In applying this procedure to intrathoracic operations involving exclusion of cardiac activity, for example, the most profound inhibition can be achieved in the cerebral cortex, which is the most sensitive to oxygen deficiency. The temperatures also fall in the lower levels of the brain, although to a smaller extent than in the upper ones. An even smaller fall in temperature is observed in the rectum. This may be ascribed to the absence of direct cooling of the trunk. The retention of a fairly high heart rate in the presence of profound hypothermia is a result of the relatively high temperature of the trunk, as compared with the brain. We found a similar effect when brain cooling was achieved by cooling carotid artery blood [5]. Apart from this, the maintenance of a fairly high body temperature, including the heart, eliminates the danger of development of ventricular fibrillation due to cold, while at the same time profound hypothermia of the brain is achieved. This feature may justify the adoption of this procedure in heart surgery, when it has been further investigated experimentally.

SUMMARY

The results of experiments with the isolated over-cooling of cats' brains are described. Deep hypothermia of the brain was achieved by its overcooling with the aid of "cold blankets". During such over-cooling the temperature of the brain is decreased more rapidly and more deeply than rectal. There is a difference in temperature between the external and internal portions of the brain. Thus, at the termination of over-cooling the temperature equalled, on the average: in the external layer of the brain (in the cortex) 18°C, in the medial layer (subcortex) 21.2°C, at the base of the brain 24.7°C and in the rectum 29°C.

Reduction of the brain temperature is associated with changes in respiration and circulation. The following incrase of the temperature results in recovery of these functions. Later, no pronounced disturbances were observed in these animals.

The method of over-cooling of the brain through the external surface of the head may be used in surgical practice.

LITERATURE CITED

[1] A. P. Golovin, Byull. Ekspti. Biol. i Med. 27, 3, 199-201 (1949).

[2] E. V. Gubler, Byull. Ekspti. Biol. i Med. 37, 2, 34-40 (1954).

[3] I. G. Zherebchenko and I. A. Peimer, Collection of Abstracts of Sci. Papers for 1950, Kirov Military Med. Acad.,* pp. 34-35, Leningrad 1953.

[4] O. A. Karpovich, "Stimulation of the muscular and nervous systems during cooling and warming the organism," Thesis,* Omsk 1950.

[5] N. V. Klykov, "Induction of hypothermia by extracorporeal cooling of blood," Shornik Nauchn. Trudov Kuban Skogo Medinstuta, Krasnodar 15, 73-81, (1957).

[6] N. I. Kochetygov, Collection of Abstracts of Sci. Papers for 1950, Kirov Military Med. Acad.,* pp. 26-27 Leningrad, 1953.

[7] Nikitinov, "Lowering the body temperature of typhoid patients by cooling the neck", M. D. Thesis,* St. Petersburg 1885.

* In Russian.

[8] B. V. Petrovsky, S. I. Babichev, and O. D. Kolyutskaya, Khirurgiya No. 9, 6-14 (1955).

[9] V. M. Pokrovsky, and V. M. Veisman, Proceedings of the XI Congress of the Sourthern RSFSR Branch, All-Union Soc. of Physiol., Biochem., and Pharmacol.* pp. 204-205 Stavropol 1956.

[10] P. M. Starkov, Proc. 26th All-Union Congress of Surgeons,* pp. 59-63 Moscow 1956.

[11] V. N. Sheinis, Freezing,* Moscow 1943.

[12] W. Bigelow, C. Callaghan, A. Donald, and Scott J. McQueen, Arch. Surg., 69, 2, 208-215 (1954).

[13] T. Fay, and G. W. Smith, Arch. Neurol. Psych., 45, 2, 215-224 (1941).

[14] T. Fay, Med. Physics, Chicago, 1224-1228 (1944).

[15] H. Swan, H. Robert, W. Virtue, S. Gilbert, and T. Kirecher, Ann. Surg. 142, 3, 382-399 (1955).

* In Russian.