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Research Article

Restoration of Respiration in Mammals Upon Cooling the Brain to 16 - 14 and Even to 4 - 1°C

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Abstract

The work is devoted to the study of vital activity of a mammal brain upon cooling an organism. The respiration of an animal submerged into icy water with its head and breathing through a tube inserted into the trachea was arrested at the brain temperature of about 19°C. At the same time, the frequency of the heart contractions abruptly slowed down. At this moment, artificial ventilation was switched on and the heart was simultaneously warmed to 20°C, which provided 30 - 40 contractions per minute to the heart and circulation in the brain. Upon further incessant cooling of the brain to 4 - 1°C with artificial ventilation the heart activity and circulation in the brain persisted for many hours. When cooling stopped, the rewarming of the whole body immediately restored the blood pressure and temperature homeostasis. This means that at the temperature 1°C the brain still retains the mechanisms of regulating its most important function - circulation.

Keywords: *Homoeothermia and Cold; Artificial Ventilation; Resuscitation of Life*

Introduction

The action of cold on humans and animals has a great number of theoretical and practical problems. Nowadays the main interest of scientists on the action of cold on homoeothermic organism is focused at the possibilities of deep freezing of humans, animals, embryo, and separate organs at the liquid nitrogen temperature (-196°C) with their subsequent resuscitation. On this basis a new branch of science – cryonics, or cryobiology, or conservation of life by cold came into being. In many works and textbooks, the authors report that a complete cessation of any energetic processes occurs in a living tissue at the temperature -100 - -130°C [1,2]. In such a case, the organism tissues retain their biological structure, which can exist eternally, since no reconstructions in their biological architecture can occur any more. The first scientist who used this axiom was professor Lui Rey. He took an embryo of a hen, exposed it for several hours at the temperature of liquid nitrogen, then at room temperature he observed rhythmical contractions of the embryo heart with the frequency as in the norm [3]. Later Ettinger repeated his experiments and wrote a book "The prospect of immortality". This book withstood 20 reprints from 1964 to 2005. In the latest version, the development of this science are summed up [4].

The aim of this work is also to study the problem of cooling a warm-blooded organism. However, our purposes are quite different. They deal with cooling the warm-blooded organisms in the temperature diapason from 36 - 38 to 4 - 1°C and revealing the viability of the brain at such low temperatures. The tissues appeared to retain the viability for a sufficiently long time at such low temperatures. This part of cryobiology occupies a relatively small volume in modern scientific investigations, but its significance is great. For the last 15 - 20 years this part of cryobiology was developing comparatively slowly, though cooling a human organism within the above-mentioned limits occurs commonly. This can happen during sea catastrophes, when working on oil platforms in Arctic, during snow avalanches in the mountains, at last as the result of fatal accidents upon assimilating Arctic and Antarctic regions. Lloyd's insurance agency every year records thousands facts of the seamen death from overcooling the body resulting from sea catastrophes. The arrest of respiration under these conditions is often the first result. In such cases the victims of hypothermia are usually sent to the morgue. The tragedy is that by a number of our and other data the victims of such hypothermia still can be resuscitated. The question arises, how much the mammal brain is tolerant to low temperatures of about 0oC, what measures must be undertook with the aim of saving the man under such extreme conditions. How long the brain may survive at such low temperature so as its vital activity could be restored and how to make it competently? These are just the questions the rescue teams for overcooling victims face most commonly.

Materials and Methods

The white rats 150 - 180g in mass were used as the test animals. The narcosis – Nembutal, 35 mg/kg intraperitoneally. The animals were fixed on a special bench. For cooling they were submerged with their head into water with ice. Respiration was performed through a rubber tube connected to the tracheotomic cannula, brought out above the surface of water. The length of the tube was 2.5 cm. The respiration movements were recorded by an electric carbon transducer on a self-recorder. The arterial blood pressure was recorded with the help of a catheter introduced into the femoral artery, of electron self-recorder, and of electron pressure gage. The heart was warmed with the help of four metal plates located on the thorax above the heart. The square of each plate was 1 cm^2. A small electric heater warmed the plates up to 48 - 49°C. The brain temperature was measured by copper-constantan thermocouple 0.3 mm in diameter, which was inserted to the depth 8 - 9 mm through parietal bones. The rectal temperature was also measured by the thermocouple at the depth 5 cm. The sensitivity of the thermal measuring devices was 0.1°C per 1 mm in the self-recorder band. A special miniature apparatus of artificial ventilation for rats was used for ventilating the lungs after cold paralysis. The gaseous respiration mixture contained 95 vol% of oxygen and 5 vol% of carbon dioxide. The volume of artificial ventilation was 100 ml/100g per minute, which is the norm for rats.

Brain tolerance for cold in common mammals

Upon gradual cooling of the head and of the whole body the respiration in rats disappears at the temperature of the brain and other organs of about 19°C [5,6]. This results in hypoxia, which increases rapidly. Eventually the animal dies from the oxygen deficit rather than from cold. Hence at the moment of respiration arrest we switch on the artificial ventilation, which results in an increase in the blood pressure and it maintains its value if we do not develop cooling to lower temperatures. In such a state at the brain and other organs temperature 16 - 14°C the animal can maintain life for several hours, whereas without artificial ventilation it would be at an absolutely deadly temperature of the brain and other organs (19-(3-5)) = 16 - 14°C. In other words, the animal tolerance for cold increases by 3 - 5°C. Artificial ventilation based on the blood saturated with oxygen not only maintains the respiration, but, what is the main thing increases the tolerance of an organism to its cooling by several degrees. This characteristic of artificial ventilation is not mentioned in the current literature. This fact must be taken into account by the rescue teams for overcooled man. The termination of further cooling and starting a careful rewarming resuscitates the animal to normal life. Therefore, it can be presumed that cooling the brain to 16 - 14°C does not disrupt its ability to regulate the circulation and resuscitate the animal life, since only the retention of corresponding mechanisms of physiological regulation of circulation in the brain structures at 16 - 14°C allows the animal life to be prolonged.

The question arises, what happens if cooling will be extended after the animal temperature decreased to 16 - 14°C. The matter is that further cooling will affect the contractile activity of the heart. The contractions weaken, the frequency of the heart contractions in a rat and other animals (and, evidently in man) decreases. This shows itself starting from the myocardium temperature decrease to 15 - 17°C and lower. With the aim of avoiding this phenomenon during restoration of the heart functioning in a deeply cooled animal and to make the heart operate and supply the brain with the blood the heart must be warmed at least to 20°C. At this temperature, the heart makes about 40 full-value contractions per minute, which is quite sufficient for supplying the cooled brain with the blood saturated with oxygen. It is sufficient since the animal at the brain temperature 4 - 1°C retains life for several hours. Oxygen plays an important role in this procedure. A high oxygen pressure in the blood is a necessary condition for its consumption by the tissues at low temperatures.

The data of our experiments are given in the table. According to these data on cooling the brain to 4 - 1°C the temperature of the heart due to its local warming increases to 18 - 20°C. Such a temperature of the heart allowed it to contract about 40 times per minute and supply the heart muscle and the brain with cold, saturated with oxygen blood. The blood pressure at this moment was, on the average, 40 mm Hg. In such a state, the animal could retain life and maintain the blood pressure for several hours at the brain temperature 4 - 1°C. Upon rewarming the body at the rectum temperature, on the average, 16.5°C the brain temperature increased to 20.5oC, the blood pressure increased, on the average, to 55 mm Hg. In four experiments, out of nine the pressure attained 60 - 75 mm Hg. The moment of switching on the artificial ventilation, the moments of switching off cooling the animal and switching off the artificial ventilation are given in the figure. The Table gives the numerical data of the temperature of brain, heart, rectum, and the blood pressure at the starting period of rewarming the animal.

№ of exp.	Exposure at minimal brain temperature					Rewarming. The time of restoration of respiration			
	Time of exposure, min	t °C of the brain	t °C of the heart	t °C of the rectum	Arterial blood pressure, mm Hg	t °C of the brain	t °C of the heart	t °C of the rectum	Arterial blood pressure, mm Hg
1	10	4	20	-	57	21	28	15	75
2	14	3	-	-	37	19	29	-	60
3	16	4	20	-	35	21	29	-	44
4	19	3	18	4	39	23	28	15	64
5	37	3	20	4	34	23	32	21	43
6	66	2	20	3	45	21	30	17	46
7	67	1	22	1	39	18	29	12	44
8	127	1	20	-	36	18	23	18	54
9	130	2	20	1	38	20	28	10	62

Table: *Temperatures of the brain, heart, rectum, and arterial blood pressure in white rats in a state of deep cooling and during restoration of spontaneous lung respiration upon rewarming the animals.*

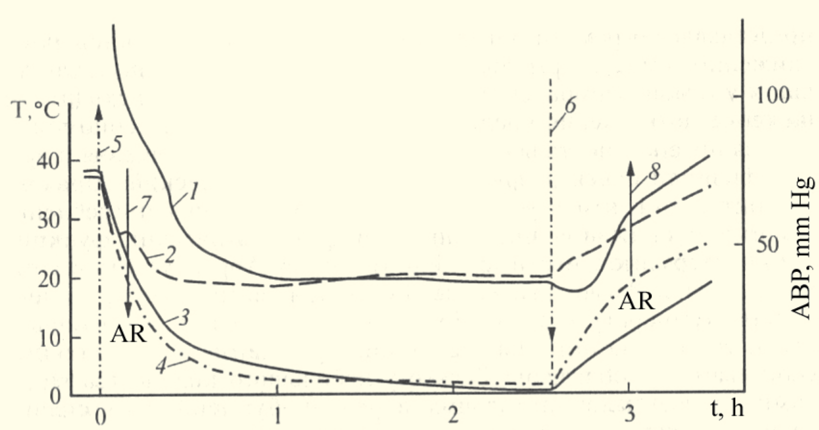

Figure: *Cooling the rat brain to 1°C under artificial ventilation and local warming of the heart retaining the arterial blood pressure at the level 40 - 45 mm Hg. X- axis – the time, h. Y-axis to the left – the temperature in the brain and in the rectum; to the right – arterial blood pressure, mm Hg. 1: Arterial Blood Pressure; 2: to of the Heart; 3: to – in the Rectum; 4: to in the Brain; 5: the Beginning of Cooling the Animal; 6: the Beginning of Warming Up; 7: Switching on the Artificial Ventilation; 8: Switching off the Artificial Ventila*tion.

The continuous recording of the most important parameters of a rat vital activity in one of the experiments is given in the figure. It can be seen that the heart temperature is maintained at the level of 18 - 20°C during the whole experiment, the arterial blood pressure is maintained at the level of about 40 mm Hg almost during the whole experiment, whereas the temperature of the brain decreases almost to 1°C in spite of warming the heart.

In the available published literature for the last 15 - 20 years we could not find any works similar to our studies of the physical stability of the brain of homoeothermic animals to cooling. In various organisms, the temperature tolerance of the brain is different. In a man, the respiration is arrested at the body temperature 25 - 27°C, in rabbits at 21 - 23, and in rats at 19°C. In this case humans and animals die from hypoxia resulting from the arrest of respiration rather than from cold. These facts are very important for recovering a man after cold paralysis of physiological functions of the brain. This fact has also a fundamental significance. It is known that the temperature thresholds of maintaining the life in our planet were rather limited in the region of high temperatures but rather wide in the regions of low temperatures. In the last few years the papers close to our topic appeared in current literature. For example, the section "Hypothermic therapy" in [7,8]. A comparatively mild, not deadly hypothermia is considered in these works. It may serve as a therapeutic factor for certain diseases and form the starting stages of adaptation of a warm-blooded organism to cold.

Conclusions

1. The brain temperature 19°C results in the paralysis of respiration and death from hypoxia. However, if at this deadly temperature the artificial ventilation is switched on, the tolerance of an animal to cold increases, it retains viability at the temperatures several degrees lower. The death barrier is overcome, and the animal retains the rhythmical work of the heart and the possibility of complete resuscitation of life.

2. Further decrease in the brain temperature to 4 - 1°C means the inevitable death of the animal under conventional conditions. However, under artificial ventilation with careful warming of the heart to 20°C we offer the heart the possibility to contract up to about 40 times per minute and supply the brain and heart with cold blood saturated with oxygen. This means that at the temperature 4 - 1°C the brain still retains its functions regulating the circulation. Such a precedent allows an important medical conclusion to be made: if in an overcooled man not only respiration but also the rhythmical heart contractions are lost, various procedures of stimulating the respiration and heart must be used after local warming of the heart.

3. The point is not only in retention of the muscle strength of the heart, the point is that upon further decrease in the brain temperature to 4 - 1°C the brain centers regulating the circulation retain a minimum of their functions. Upon rewarming the body and increasing hypoxia they reflectively support the inflow of the blood and oxygen to the brain.

4. The possibility of life and regulation of circulation in a homoeothermic organism at the brain temperature of about 1°C and restoration of temperature homeostasis under these conditions creates an important precedent of saving an organism from death, when it is cooled to such an extent. Moreover, this fact expands the limits of our knowledge about the temperature dependence of physiological functions of the tissues of warm-blooded animals. A characteristic feature is that the tissues of these animals perpetually functioning during the whole life at a strictly constant temperature 35 - 38°C usually die as the body temperature decreases by 13 - 15°C, yet not from cold, but from oxygen deficit, since the system of their oxygen supply for some reasons cannot operate effectively at such a decrease in the body temperature without artificial ventilation. Rats and other mammals are capable of retaining the viability and vital activity at the brain temperature of about 1°C, if their heart works and oxygen is supplied with the blood with the help of artificial ventilation. It is a striking fact that the organs and cells of warm-blooded animals are capable of surviving for some time at a temperature close to liquid nitrogen (-196°C) [4]. It is believed that the retention of viability of the tissues of brain and other organs of warm-blooded organisms at such low temperatures is one of the reasons and mechanisms of generation and development of the animated world in the cold intergalactic spaces of the universe.

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