RESTORATION OF HIGHER NERVOUS ACTIVITY IN DOGS RESUSCITATED AFTER 30-MINUTE CLINICAL DEATH IN CONDITIONS OF HYPOTHERMIA

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Many authors [1-8] have studied the disturbance to the highest sections of the brain after different periods of clinical death caused by acute blood loss and the extent of their functional restoration. T. S. Fedotov [6], V. D. Yankovsky [7], N. N. Sirotinin [5], L. I. Mursky and V. K. Ustinova [2] and others conducted experiments under ordinary conditions of temperature. Recently, the duration of clinical death has been successfully lengthened to 1 hour [4] by means of hypothermia in the animals suffering the acute blood loss. It is still not clear how much the higher sections of the central nervous system suffer in dogs resuscitated after lengthy periods of clinical death in conditions of hypothermia. The purpose of this work, therefore, was to determine how higher nervous activity changed in 4 dogs, which were resuscitated after 30-minute clinical death caused by acute blood loss in conditions of general body cooling.

EXPERIMENTAL METHODS

The experiments were conducted on 4 male dogs weighing from 17.5 to 21.5 kg. Before the experiment, the animals were injected with a 2% solution of pantopon, in a dose of 2 ml per 5 kg of weight and with 1 ml of a 0.1% atropine solution. Body temperature was reduced by physical cooling combined with an intravenous injection of a 0.2% pentothal solution. Clinical death was caused by massive blood-letting from the femoral artery. The vital functions were restored in the animals by means of a complex resuscitation method developed by V. A. Negovsky. Fibrillation, when it occurred, was eliminated by single condenser discharges (according to N. L. Gurvich's method). After cardiac activity had been restored, the animals were warmed by immersion in warm water (43-45°). In order to determine the extent to which the functions of the cerebral cortex had been restored in the resuscitated animals, a system of conditioned reflexes had been previously developed according to a stereotype consisting of 5 positive stimuli (metronome 120, light, bell, light, metronome 120) and one inhibitory stimulus (metronome 60). The acid-defense method was used in these experiments. An 0.3% solution of hydrochloric acid was used as the unconditioned stimulus.

EXPERIMENTAL RESULTS

The animals were bled when their body temperature was from 25.8° to 26°. Clinical death lasted 30 minutes. The dying period on a background of cooling lasted from 9 minutes, 35 seconds to 26 minutes. At the time of resuscitation, body temperature in the animals was reduced to 23.8-25°. Heart action in the dogs was restored after intervals of from 1 minute, 13 seconds to 4 minutes, 30 seconds. The later heart action restoration was caused by the appearance of fibrillation during the first stage of resuscitation. Respiration was restored after intervals of from 7 minutes, 23 seconds to 58 minutes, 55 seconds. The corneal reflex was restored 35 minutes, 30 seconds to 46 minutes, 25 seconds after the beginning of resuscitation. The animals were warmed for 1 hour,

90 minutes from the beginning of resuscitation; after this warming period, the body temperature was 31-32°, and after 13-15 hours, it was as high as 37.2-37.6°. The animals were in a somnolent condition during the first 9-14 hours after resuscitation. Their vision and hearing were restored after 9 1/2 -16 hours, and after 16-21 hours, they began to walk and to take food independently. The animals' condition was completely satisfactory by the end of the first day after resuscitation was begun; by the 2nd day, their outward behavior was approximately the same as that of healthy animals. Before the experiment, the first conditioned reflex reaction to the metronome 120 appeared after the 7th combination in the dog August, to the light, from the first combination, and to the bell, after the 7th combination. The differentiation began to be developed after the 7th use of the inhibitory stimulus. The state of the conditioned reflexes in the dog August before resuscitation is given in the report of Experiment No. 85. Sixteen hours and forty-five minutes after resuscitation, August was taken into the conditioned reflex chamber. The data obtained from the first three experiments after resuscitation show that higher nervous activity was disturbed in these dogs, although there were no noticeable changes in their general behavior.

Note the low level of the conditioned reflexes in the first experiment after resuscitation (Experiment No. 1).

No. Experiment and date	Time exp. (in hrs. and min)	Ordinal No conditioned stimulus	Conditioned stimulus	Time conditioned stimulus acted alone (in sec.)	Magnitude conditioned reflexes (No. drops) total	Magnitude conditioned reflexes (No. drops) for each 5 sec.	Latent period conditioned reflexes
Before clinical death							
85 May 23,1955	12:25	236	M_{120}	20	1	1 –0—2—1	5
	12:28	81	Light	20	5	2--0—0—1	3
	12:31	90	M_{60}	30	--	—	-
	12:34	92	Bell	20	3	0—1—1—1	9
	12:37	82	Light	20	2	1—0—0—1	4
	12:40	237	M_{120}	20	3	0—1—1—1	7
After resuscitation							
1 May 25,1955	10:25	1	M_{120}	20	1	0 0—1—0	14
	10:28	1	Light	20	-	—	-
	10:31	1	M_{60}	30	1	0 0 1—0 - 0—0	—
	10:34	1	Bell	20	--	—	—
	10:37	Saliva funnel torn off				--	—
2 May 25,1955	15:40	2	M_{120}	20	1	0- 0 - 0--1	18
	15:43	2	Light	20	8	2—6 - 0—0	4
	15:46	2	M_{60}	30	5	4 - 1—0—0—0--0	—
	15:49	2	Bell	20	--	—	--
	15:52	3	Light	20	12	2 0 4 6	4
	15:55	Funnel torn off					
3 May 27,1955	15:45	3	M_{120}	20	1	0 1 - 0 -0	8
	15:48	4	Light	20	1	0—1—0—0	7
	15:51	3	M_{60}	30	31	3--13 12 -6 -0—0	--
	15:54	3	Bell	20			
	15:57	5	Light	20	3	0 0 - 3 - 0	14
	16:00	4	M_{120}	20		—	—
17 June 16,1955	15:20	34	M_{120}	20	7	1—3—3--9	5
	15:23	36	Light	20	3	0--1—1--1	9
	15:26	16	M_{60}	30			—
	15:29	16	Bell	20	2	0 0--1--1	14
	15:32	37	Light	20	4	0--1--1--2	5
	15:35	35	M_{120}	20	3	0 1 -1 1	8

After the bell, the dog manifested a strong motor excitation, during which he tore off the saliva funnel.

Forty hours after resuscitation (Experiment No. 2), the animal was somewhat calmer during the experiment; the conditioned reflex stereotype, however, was not yet completely restored. The most noteworthy fact was the paradoxical behavior of the nervous system in response to stimuli which had caused an adequate reaction before the clinical death. On the third day (Experiment No. 3), the character of conditioned reflex activity was approximately the same as on the second day, but the appearance of an ultraparadoxical phase was observed.

On the 4th day after resuscitation (Experiment No. 4), a single eradication of the conditioned reflexes to the metronome 120 was done.* This caused conditioned reflex activity to improve; the tonicity of the cerebral cortex cells was raised, and the conditioned reflexes began to become stable. Bromine was used during the 5-day rest period after the 12th experiment (on the 17th day after resuscitation) in order to improve the correlation of the principal nervous processes. The animal received 0.6 g of bromine with milk on the first day and 1.8 g, fed twice a day, on the following days. The results obtained from the use of bromine are shown in the Table (Experiment No. 17). Therefore, the use of bromine gave positive results. The differentiation was strengthened, and the character of conditioned reflex activity became almost normal. Of course, the normalization of conditioned reflex activity was connected with the time which had elapsed since the moment of resuscitation as well as with the bromine treatment.

A similar picture of activity restoration in the higher sections of the brain after 30-minute clinical death in conditions of hypothermia was observed in the other three experimental animals – Baikal, Ruslan and Treasure. Differences were observed, however, during the beginning of restoration (hypnotic phases absent) and during the administration of the bromine preparations, which had to be used in all of the dogs. This much is clear: that the more vulnerable process of inherent inhibition is the process most weakened by conditions of clinical death. That the stimulation process was also considerably weakened was shown by the fact that experiments in the conditioned reflex chamber could not be done daily, since this caused the progressive exhaustion of the cerebral cortex cells. Our dogs had very different types of higher nervous activity. This is the reason why, in the experiments using sodium bromide, Baikal (weak variant of the strong type) was given sodium bromide, for 4 days in doses of 0.5-0.6 g, while Ruslan, a strong, balanced, mobile type, received an average of 3 g of sodium bromide daily for 6 days, and Treasure, which had an extremely weak type of higher nervous activity, was given 0.1 g of sodium bromide daily for 20 days.

All of the experimental dogs lived. Their higher nervous activity was completely restored 13-23 days after the start of resuscitation.

Therefore, our study of higher nervous activity restoration in dogs after 30-minute clinical death caused by lethal blood-letting under conditions of hypothermia showed that the conditioned reflexes could be completely restored in the dogs; there were, however, different disturbances of the relationships between the principal nervous processes in the different animals during their restitution. These disturbances were either manifested by extremely acute functional exhaustion in the higher sections of the central nervous system or by a hypnotic condition expressed to varying degrees in the animals from slight, compensating relationships to extremely pronounced forms of an ultraparadoxical phase.

SUMMARY

The characteristic features of recovery of the function of the brain cortex after resuscitation was studied in 4 dogs. For that purpose a system of conditioned reflexes was previously developed. These reflexes were formed according to a stereotype, consisting of 5 positive (metronome – 120 light, bell, metronome –120) and one inhibitory (metronome –60) stimulants. The acid-defense method was used in these experiments. The possibility of complete recovery of the previously developed conditioned reflexes after a 30-minute clinical death, caused by acute blood loss in condition of hypothermia was proved in these animals.

Various disturbances of relationship between the fundamental nervous processes took place during the process of recovery.

These disturbances were either in the form of extreme exhaustion of the functions of the highest portions of the central nervous system, or gave the picture of various degree hypnotic condition.

*Our experiments have shown that this method often strengthens the process of inherent inhibition.

LITERATURE CITED

[1] A. R. Kotovskaya, Abstracts of the Reports Given at the Yub. Scientific Session for the 200th Anniversary of the First Moscow Medical Institute (in Russian), Moscow, 1955, pp 26-27.

[2] L. I. Mursky, and V. K. Ustinova, Byull. Eksptl. Biol. i Med., 1954, Vol. 38, No. 12, pp-19-22.

[3] V. A. Negovsky, A. I. Makarychev and A. V. Popova, I. P. Pavlov Zhurn. Vysshei Nerv. Deyatel., 1956, Vol. VI, No. 4, pp 584-598.

[4] V. A. Negovsky and V. I. Soboleva, Arkh. Patol., 1956, No. 6, pp. 68-70.

[5] N. N. Sirotinin, V. D. Yankovsky, The Physiology of the Nervous Processes, (in Russian), Kiev, 1955, pp. 123-130.

[6] T. S. Fedotov, Byull. Eksptl. Biol. i Med., 1941, Vol. 11, No. 2, pp.186-189.

[7] V. D. Yankovsky, Problems of Physiology (in Russian), 1954, No. 8, pp-51-63.

[8] J. Malmejac, P. Plani and E. Boguert Compt. rend. Soc. Biol., 1954, v. 148, N 1-2, p. 85-88.