

# THE EFFECT OF HYPOTHERMIA COMBINED WITH HIBERNATION ON CONDITIONED REFLEXES FROM THE AUDITORY ANALYZER

G. V. Khvedelidze

Institute of Experimental and Clinical Surgery and Hematology  
(Director, Academician of the Academy of Sciences of the Georgian SSR K. D. Eristavi)  
Academy of Sciences of the Georgian SSR, and Physiological Laboratory,  
Faculty of Pediatrics (Director, Corresponding Member of the Academy of Sciences of  
the Georgian SSR Professor D. M. Gedevarishvili), Tbilisi Medical Institute  
(Director, Professor P. G. Gelbakhiani)  
(Presented by Academician V. N. Chernigovskii)  
Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*,  
Vol. 53, No. 6, pp. 32-35, June, 1962  
Original article submitted July 26, 1961

Little research has been done into the effect of hypothermia on conditioned reflexes [5, 6, 7]; moreover, some of this has been undertaken to study the effect of hypothermia on conditioned reflexes during the cooling process. So far as the sequelae of a single exposure to hypothermia are concerned, i.e., the investigation of possible residual disturbances of higher nervous activity of an animal which has fully recovered from hypothermia (for example, on the day after cooling), only two papers by Soviet writers are devoted to this problem [6, 7]. In several investigations by foreign workers this problem has been studied by the method of free movements, by observation of the behavior of animals recovering from hypothermia, or by comparison of the electroencephalographic findings before and after hypothermia [8-11, and others]. Nevertheless, from the clinical point of view it is of the greatest practical importance to elucidate this problem rather than study the dynamics of the higher nervous activity during cooling.

L. I. Murskii [7] observed a disturbance of both positive and negative salivary reflexes to acid in dogs after hypothermia. These were restored gradually after the 4th-5th day following hypothermia, which was usually induced without "cocktail" combinations and in association with exsanguination in order to develop a state of clinical death in the animal; in some experiments only drugs such as pantopon and atropine were given. O. A. Karpovich [6] found no disturbances of the positive motor-defensive conditioned reflexes on the second day after hypothermia (the rectal temperature was taken to 25-27°) in conjunction with morphine anesthesia. Karpovich did not study the effect of hypothermia on internal inhibition (differentiation).

## Experimental Method and Results

In our experiments on dogs, besides hypothermia we also used pharmacological agents in the form usually given in surgical practice (anesthetics, "cocktails"). We studied both positive and negative conditioned salivary reflexes.

Unilateral conditioned salivary reflexes to the sound of a metronome (180 beats per minute) were formed in 2 dogs with reinforcement by electrical stimulation of a tooth by D. M. Gedevarishvili's method [1-4]. At the present time this may be regarded as the easiest and the most convenient and accurate method of study of conditioned reflex activity in the case of unilateral reflexes. It is impossible to achieve such a constant reaction as is obtained by electrical stimulation of a tooth by means of the methods of food reflexes, motor-defensive, or acid-salivary reflexes.

For example, in our experiments in response to the unconditioned electrical stimulation of a tooth one dog (Dzhek) always produced 12-14 drops of saliva, and another (Roza) produced 10-12 drops. This ensured constancy of the conditioned secretion. After consolidation of the conditioned reflexes (in Dzhek after 30, and in Roza after 40 combinations) Dzhek produced 8-10 drops of saliva in response to the conditioned stimulus, and Roza produced 7-8 drops. The conditioned and unconditioned stimuli were combined for a period of 20 seconds.

Differentiation was then established to the sound of a metronome giving 90 beats per minute. Stable differentiation was produced in Dzhek after 18 applications of the negative stimulus without reinforcement by stimulation of a tooth, and in Roza after 26 applications. The negative stimulus was applied twice on each day of the experiment.

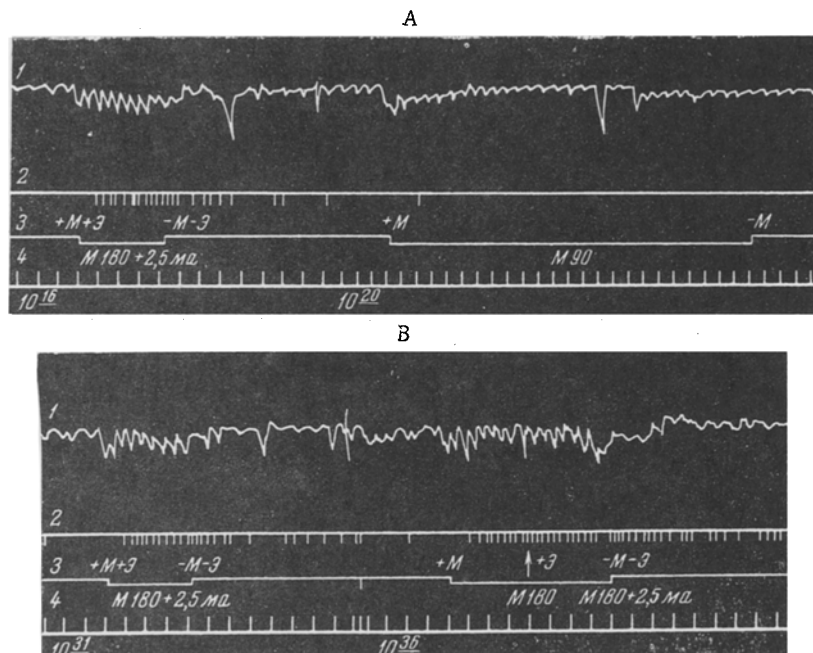


Fig. 1. Kymograms of the conditioned-reflex activity of the dog Roza on the second day after hypothermia. A) Unconditioned stimulation of a tooth in conjunction with the sound of a metronome (180) causes secretion of saliva; the sound of a metronome (90) (differential stimulus) causes no salivation; +3) application of electrical stimulation to a tooth; -3) discontinuation of electrical stimulation; +M) metronome on; -M) metronome off; B) unconditioned stimulation of a tooth in conjunction with the sound of the metronome (180) causes the secretion of saliva; the sound of the metronome (180) (positive stimulus) causes appreciable salivation. Significance of the curves (from above down): respiration; sialogram — registration of drops of saliva from the parotid duct; time marker (5 seconds). The arrow indicates the moment of switching on the electric current.

The resulting differentiation was so well developed that on a given day of the experiment Dzhek produced no saliva whatever in response to the negative, inhibitory stimulus applied for 2 minutes, yet produced 12 drops in response to the positive stimulus. Roza secreted 1-2 drops of saliva in response to the inhibitory stimulus and 7-8 drops in response to the positive stimulus.

Having obtained a firmly established temporary connection (a positive conditioned reflex) and accurate differentiation (internal inhibition) in the experimental dogs, we could easily test the effect of one or two exposures to hypothermia (at an interval of one week) on the fundamental central nervous processes — cortical excitation and cortical inhibition.

In order to produce hibernation with hypothermia, 1.5 ml of 5% promedol was injected intramuscularly, followed 30 minutes later by intramuscular injection of a "cocktail" consisting of the following mixture in a dose of 0.1 ml/kg body weight: 50 ml of 0.1% atropine sulfate, 1.0 g dimedrol, 1.0 g chlorpromazine). Ether anesthesia was induced after a further 15-20 minutes; the dog was then placed in a bath of water with cooling mixture (potassium thiocyanate mixed with finely crushed ice in proportion of 1:10). On the first occasion hypothermia in the dog Dzhek was carried to a rectal temperature of 24°, and on the second (one week later) to 23°. In experiments on the dog Roza, hypothermia was carried once to a rectal temperature of 24°. A thermogalvanometer was used to measure the rectal temperature.

When a rectal temperature of 23-24° has been attained, the dog was left in the bath without cooling mixture for a further 25-30 minutes, after which it was placed in a bath of warm water (36-38°). When the rectal temperature reached 33-34° the dog was taken from the bath, carefully dried, and kept in a warm room by a stove until next morning. After 2-2½ hours the rectal temperature regained its initial level (as before hypothermia), i.e., 37-38°.

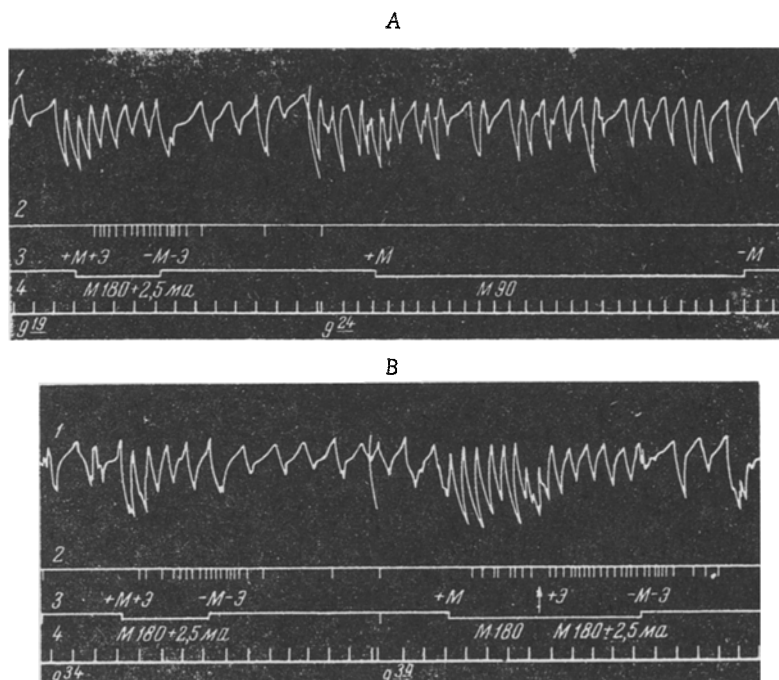


Fig. 2. Kymogram of the conditioned-reflex activity of the dog Dzhek on the second day after a second exposure to hypothermia. Legend as in Fig. 1.

On the second day after hypothermia the dogs reacted as usual to both the inhibitory and the positive stimuli. It may be seen in Figs. 1 and 2 that differentiation was not impaired after hypothermia (no saliva — zero differentiation — by the dog Dzhek, one drop by the dog Roza in response to the negative conditioned stimulus). No disturbance of the response to the positive conditioned stimulus was observed (8 drops of saliva in Dzhek and 9 drops in Roza). Differentiation and the positive conditioned reflex were likewise undisturbed after a second exposure to hypothermia one week later in the experiments on the dog Dzhek.

It is possible that if more delicate forms of differentiation and complex conditioned reflexes were established and all the unique features of the higher nervous activity were studied, some changes in the cortical activity might be detected after hypothermia.

As suggested explanation of the disturbance of the higher nervous activity described by L. I. Murskii [7] after hypothermia is that it might have been caused by the particularly severe experimental conditions associated with the marked anoxia during the period of clinical death.

#### LITERATURE CITED

1. D. M. Gedevanishvili (Gedevani). Address to the Third Scientific Conference of the Tbilisi Institute [in Russian], 1947.
2. D. M. Gedevanishvili and G. L. Vepkhvadze, The Paired and Individual Working of the Cerebral Hemispheres [in Russian], Tbilisi, 1956.
3. D. M. Gedevanishvili and G. L. Vepkhvadze, In: Problems in the Physiology of the Central Nervous System [in Russian], p. 185, Moscow-Leningrad, 1957.
4. D. M. Gedevanishvili (Gedevani). Theses and Abstracts of Proceedings of the Eighteenth Conference on Higher Nervous Activity [in Russian], No. 1, p. 50, Leningrad, 1958.
5. V. K. Gubenko, The Effect of Experimental Cooling on Conditioned-Reflex Activity and Certain Vegetative Functions [in Russian], Candidate dissertation, Stavropol', 1956.
6. O. A. Karpovich, In: Problems in Acute Hypothermia [in Russian], p. 37, Moscow, 1957.
7. L. I. Murskii, The Physiology of Hypothermia [in Russian], Yaroslavl', 1958.
8. J. Callaghan, D. McQueen, J. Scott, et al., Arch. Surg., v. 68, p. 208 (1954).
9. J. Malméjac and P. Plane, Bull. Acad. nat. Med., (Paris), v. 139, p. 37 (1955).
10. J. Malméjac, P. Plane, and E. Bogaert, Comptes rend., Acad. Sci. (Paris), v. 242, p. 2764 (1956).
11. J. Malméjac, P. Plane, and C. Malméjac, J. Physiol (Paris), v. 48, p. 632 (1956).