COURSE OF CAMPHOR EPILEPSY IN CONDITIONS OF HYPOTHERMIA

COMMUNICATION I CHARACTERIZATION OF INHIBITION OF THE CENTRAL NERVOUS SYSTEM IN HYPOTHERMIA

R. B. Tsynkalovsky and Ya. I. Azhipa

From the Department of Pathophysiology (Chairman-Prof. A. N. Gordienko)
Rostov Medical Institute (Director-Prof. G. S. Ivakhnenko)

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For the genesis and course of an epileptic fit induced experimentally by various means (freezing of a section of the cortex, loud noise, camphor, cardiazole, bile), of basic importance is the state of the inhibitory and stimulatory processes in the central nervous system. Intensification of inhibition makes more difficult the development of experimental epilepsy, and intensification of stimulation contributes to its development. Consequently, the particular features of the genesis and course of an epileptic fit enable one to judge to a certain extent the mutual relations of stimulation and inhibition in various states of the organism.

The present investigation sought to give a characterization of inhibition of the central nervous system upon hypothermia on the basis of the peculiarities of the genesis, course and outcome of epilepsy with a different degree of chilling. For this purpose, we used camphor epilepsy since it is easily induced in hypothermia [10], while the convulsive states in chilled animals cannot be obtained with other means [5, 9].

EXPERIMENTAL METHODS

The experimental animals were cats and dogs. The different degree of hypothermia (19-25°C — with intrarectal measurement) was obtained by casing the animal in ice. Epilepsy was induced by intravenous introduction of 20% camphor, diluted by ether at the ratio of 4:1 on the basis of 0.5-2 ml per 1 kg body weight in the dogs and 0.3-1.0 in the cats.

EXPERIMENTAL RESULTS

The epilepsy induced in the nonchilled animals by intravenous introduction of camphor usually began within 0.5-1 minute and lasted at the most for 3 hours. The pattern of the epileptic fit consisted of: motor aura, convulsions, salivation, munching, exophthalmos, involuntary urination and defecation, change in blood pressure and respiration. The aura was sometimes absent and the epilepsy began with convulsions. The convulsions were of a clonicotonic nature, the fits came at intervals during which it was possible to observe different forms of motor excitation. Doses of 1-2 ml of camphor per 1 g of animal weight produced a state of severe epileptic status which led to a comatose state with subsequent death. Usually after introduction of a dose of 0.3-0.5 ml camphor per 1 kg weight, the fit terminated with recovery.

Hypothermia was characterized by a number of changes, most pronounced of which was inhibition of the central nervous system, leading in the last analysis, as is known, to the creation of a deep general anesthesia, unobtainable by means of existing narcotic substances. Taking this into account in 12 experiments on dogs, whose body temperature was lowered to 25-22°C by chilling, we used in order to induce epilepsy a dose of 2 ml, considering that a dose of 0.5 ml would be ineffective in such a state.

The results of the experiments showed that in the animals, independent of the degree of hypothermia, with doses of 2–1 ml, an epileptic status developed with a transition to the typical epileptic fit which continued for some hours and terminated with the emergence of the animal from the state of hypothermia and recovery.

In one case, an animal with a temperature of 23°C died immediately after the introduction of camphor, which produced two convulsive fits.

The subsequent experiments (5 dogs) showed that a 0.5 ml dose also produced an epileptic fit differing little from the epileptic fit in normal animals.

Consequently, the different degrees of hypothermia in the dogs did not prevent development of epilepsy with the introduction of large and small doses of camphor, but saved the animals from death which regularly occurred in the nonchilled animals upon introduction of large doses of camphor.

In cats, camphor epilepsy was obtained upon reduction of the body temperature to 21–19°C (12 experiments). The results of the experiments with introduction of camphor in doses of 0.3–1 ml per kg body weight not only confirmed the possibility of development of typical epilepsy on the basis of deep hypothermia, but made it possible, as in the experiments on dogs, to reveal a number of peculiarities of its genesis and course in the chilled animals.

In a state of deep hypothermia, we often observed in the animals a prolongation of the latent period. With this, the epileptic fit, as in the nonchilled animals, began with motor aura and not infrequently, directly with convulsions. The duration of the fits increased sharply, in some experiments reached 12–16 hours, on the average lasting 2–3 hours. Thus, for example, the epileptic fit in 2 cats which were given camphor at a body temperature of 19 and 20°C with 1 ml per kg body weight lasted for 16 hours, and in one of them even for 18 hours slight fit-like twitching of separate muscles of the forelimbs and neck was witnessed. Despite the severe and prolonged course of the affection, in the animals with hypothermia, after cessation of the fit, only some depression was observed, and after a day they were indistinguishable from the healthy ones in behavior and general condition.

It is interesting that the intensity of the fits exceeded those in the experiments without hypothermia and the fits recurred at surprisingly regular time intervals, becoming toward the end increasingly rare and weak.

Thus, chilling of the dogs to 25–22°C and cats to 21–19°C did not prevent development of epilepsy upon intravenous introduction of camphor and did not change the structure of the epileptic fit, but increased the latent period and duration of the course of the fit and also its intensity. Hypothermia basically influences the outcome of epilepsy just as epilepsy changes the outcome of hypothermia, and while each of these pathological processes in isolation in given conditions ends in the death of the animals, the combination of them in that sequence which took place in our experiments led, as a rule, to recovery.

Although increase in body temperature in the excessively chilled animals with epilepsy may be completely attributable to heat production as a consequence of intense contraction of the large mass of the muscles, subsequent restoration of heat regulation on the one hand, and a favorable outcome of epilepsy that would otherwise result in certain death on the other, still require explanation.

The possibility of obtaining experimental epilepsy with camphor in conditions of deep hypothermia, that is, prolonged epileptic status with subsequent survival of the animals, particularly after introduction of large doses of camphor, is rather astonishing, since it has been firmly held that "cold" narcosis, by reducing the excitability of the central nervous system, makes it insensitive or little sensitive to all stimuli acting reflexly or directly on its cells [1, 2, 4, 6, 9].

This very fact indicates a basic difference between inhibition of the central nervous system in hypothermia on the one hand, and narcotic inhibition and also inhibition upon shock on the other, since it is known that narcosis removes epileptic convulsions and with a prolonged effect saves the animals from death. (In our experiments hexenal narcosis had the same effect as ether, curtailing the fits or preventing them from developing; in severe pleural-pulmonary and peptone shock, epilepsy did not develop).

It is well known that inhibition of the central nervous system in hypothermia is classified as prohibited. In accordance with the findings of E. V. Maistrach [4], changes in the nervous activity here are similar to those which arise with narcotization by typical narcotics (rapidity of development of inhibition, its sequence, starting from the higher sections of the nervous system, removal of subordinating influences of the upper sections of the

brain). It is known that inhibition with narcosis, shocks and other traumas to the organism, also belong to the category of prohibited. It is clear that this term, reflecting the superficial and most general aspect of inhibition, which can be demonstrated, for example, by the method of conditioned reflexes and electroencephalography, does not indicate its particular nature in each concrete case. The use of such a stimulus as camphor made it possible to clarify certain specific aspects of inhibition with hypothermia, thoroughly distinguishing it from the state of the central nervous system upon narcosis and shocks. The essence of inhibition with hypothermia is not clear; only obvious is its exclusively expedient aspect, which ensured maintenance of the nerve cells even after 12–16 hours of chaotic and excessive work. It is necessary to assume that hypothermia inhibition does not involve the pessimum, and therefore should not be prohibited. Otherwise such a powerful stimulus as camphor would not be in a position to produce excitation leading the animals to epilepsy.

Just as is the case with this type of inhibition, a characteristic of hypothermia is a fall in the excitability of the nervous system and its tonus. However, while with narcosis and shock extreme stimuli may involve the death of the animals, in hypothermia, extreme stimuli, in our case camphor, raise the tonus of the central nervous system and reduce its threshold of excitation. Physiologists in studying hypothyroidism and ageing have come across a similar state of the nervous system. It may be to a certain extent indentified with inhibition upon hibernation, ensuring economy in expediture of the energy reserves of the nerve cells. If this is really so, then inhibition in hypothermia, not being depressive, is preservative and hence more useful and physiological than protective inhibition with narcosis, shocks, etc.

Naturally, there arises the question as to which sections of the nervous system respond to the stimulation applied by camphor introduced intravenously. According to the findings of the A. D. Speransky Laboratory [3, 7, 8], an epileptic fit is the result of an intense outburst of subcortical excitation, without being restrained by the inhibitory influences of the cortex. With hypothermia, even in the initial and middle stages, the associative functions of the cortex are inhibited, and at a temperature of 25°C and less suppression and disappearance of convulsive reactions on electrical stimulation of the cerebral cortex take place [9].

It is known that the degree of inhibition of the subcortical formations in hypothermia in different conditions is weaker than inhibition of the cortex.

The foregoing gives some grounds for considering that the development of camphor epilepsy with hypothermia is associated with stimulation of the subcortical centers by the reflex or automatic effect of camphor. The question of the mechanism of the action of camphor will be studied in the next communication.

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* In Russian.