discharge principally in the same way as in the animal experiments.

In all treatments the patients were given a light evipan anaesthesia (5 mg/kg), saturated with oxygen and paralyzed by an adequate dose of succinylcholine iodide. The shock was delivered by a "Konvulsator III" according to v. BRAUNMÜHL. The cerebral electrical activity was recorded by a six-channel Grass electroencephalograph. The position of the recording electrodes are shown in Figure 1. One or two treatments were first given without xylocain in order to estimate the duration of the post-stimulatory cortical after-discharge, which was found to be fairly constant from treatment to treatment in the same patient. The dose of intravenously injected xylocain ranged between 2–4 mg/kg and a supramaximal shock was delivered 2 min after the end of the injection. The dosis of xylocain ranged between 2–4 mg/kg injected intravenously during 1 min and a supramaximal shock was delivered 2 min after the end of the injection.

Figure 1 *A–E* show the electroencephalograms during the course of an unmodified treatment. Record *A* shows the EEG. prior to any injections. Evipan and succinylcholine were then administered and record *B* shows the EEG. immediately before the shock. The shock was then delivered through bitemporal electrodes and the following records (*C* and *D*) show the after-discharge 10 s (*C*), and 25 s (*D*), after the cessation of the repetitive stimulation. Record *E* shows the spontaneous cessation of the cortical after-discharge and the post-epileptic depression of the cortical activity 1 min 40 s after the end of the shock.

Records A_1–E_1 in Figure 1 are from the same patient and show the effect of an intravenous injection of 3 mg xylocain per kilogramme. The extracts from the EEG. are taken at the same intervals. Record C_1 shows the convulsive activity which is more regular and monotonous than in the corresponding curve above. Record D_1 shows that the after-discharge was blocked 25 s after the end of the stimulus. In record E_1 there is already a restitution of pre-treatment activity.

In the present series the duration of the after-discharge was reduced by 60–80% following pre-treatment administration of xylocain. There was no certain tendency to a greater effect when the dosage of xylocain was increased to 4 mg/kg.

The EEG. was regularly followed for 30 min after the shock. In Figure 2 the EEG. is shown immediately after (*A*; A_1) and 3 (*B*; B_1), 10 (*C*; C_1) and 20 min (*D*; D_1) after the end of the after-discharge without (upper row: *A–D*) and with (lower row: A_1–D_1) xylocain. Without xylocain, there was a greater degree of depression of the cortical activity following upon the longer after-discharge than after a xylocain injection, and probably a more pronounced dysrhythmia with slow waves.

There were no complications and no complaints from the patients which could be ascribed to the xylocain treatment. It should be pointed out, however, that the intravenous use of the drug must be handled with great care until more experience has been collected.

The experiments were made in order to elucidate the significance of the after-discharge for the clinical effects of electric convulsive treatment.

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Zusammenfassung

Es hat sich gezeigt, dass Xylocain in kleinen intravenösen Dosen die epileptiformen Nachentladungen bei Elektroschockbehandlung abkürzen kann. Die Untersuchungen werden fortgesetzt, um die Bedeutung der Nachentladungen für die klinischen Effekte der Elektroschockbehandlung zu beleuchten.

Insulin and its Possible Role in the Artificial Hibernation

Artificial hypothermia or hibernation has been studied during recent years as a means of reducing the oxygen consumption of the tissues and thus allowing surgical treatment of various cardiac and vascular diseases. It is known, however, that the decrease of body temperature in the homeothermic organism is constantly followed by metabolic and cellular changes of importance. The need was therefore emphasized of reducing such disadvantages by various techniques and drugs[1]. Substances with a ganglioplegic action have acquired a special importance in this field. Such drugs reduce the changes produced by the body hypothermia but do not prevent some of the reactions of the homeotherm to the hibernation.

In fact, in animals treated with such drugs, some rather important changes of certain physiological constants have been observed (glycaemia, lipaemia, heart rate, endocrine activity), as well as the presence of shivering and shock post-hibernation, which has not yet been given a clinical or experimental explanation[2]. As a matter of fact, a homeotherm organism reacts to any decrease of body temperature with an increased metabolic rate and an increase of the organic combustions with the object of keeping its own temperature constant. In this way not only its lipidic and glycidic reserves but also the proteic ones and its enzymatic patrimony are wasted.

Having regard to these facts, it seems to us that the ganglioplegics are not sufficient to prevent the dangerous increase of organic combustions, and that it is therefore necessary to act directly on the cellular metabolism by means of some substances possessing an antagonistic action on the hormones of which production is stimulated by hypothermia. Our attention was drawn to insulin.

In fact, insulin decreases the blood sugar, increases the hepatic and muscle glycogen (which disappears rapidly with the hypothermia), favours lipogenesis, diminishes the use of O_2 by the tissues, showing a clear anabolic and hypothermic action. Such a conception has also been supported by the fact that in the hibernant

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animals (hedge-hog, hamster, etc.) the physiological decrease of their body temperature during the winter lethargy is accompanied by a hyperactivity of the endocrine pancreas, by an hypertrophy of the islands of Langerhans and an increase of the β-cells, by a strong hypoglycaemia, and by a decrease in thyroid, hypophysis and adrenal gland activity[1].

Experiments were made[2] on rabbits and dogs in order to study first of all the hypothermic action of insulin, of ganglioplegics and of both these substances used together; and secondly to study the behaviour of the animals hibernated in insulinic hypoglycaemia.

The experiments were made on 64 rabbits and on 21 dogs. The animals were divided into two groups, those of the first group were kept at room temperature while the animals of the second group were hibernated at 20–24°C with pads containing a refrigerated alcohol solution at – 5– – 10°C.

The results obtained may be thus summarized:

(A) *Animals kept at room temperature*

(1) In rabbits treated with 5 U. of insulin we noticed a decrease of temperature 0·6–4·5°C. Almost all animals showed hypoglycaemic convulsions.

(2) In rabbits treated with a cocktail of autonomic blocking agents (mefedina 0·5 mg, fargan 0·25 mg, largactil 2 mg pro kg of weight) we noticed a decrease of temperature of 0·5–2°C.

(3) The hypothermia was remarkably increased by adding insulin to the cocktail with ganglioplegic action. In animals thus treated we noticed a decrease of temperature of 4·4–7·7°C. In these animals, after administering glucose, a rapid return of the temperature to the normal values was noticed; which did not happen in animals treated with ganglioplegics only.

(B) *Refrigerated animals*

(1) No remarkable difference in speed of the lowering of temperature was noticed whether the animals had been hibernated in hypoglycaemia or not. This is probably due to the severity of the cooling (enormous number of calories drawn from the cold pads) and also to its speed (40 min to 1 h for the rabbits; 1–3 h for the dogs). It was instead constantly observed that if two animals were hibernated at the same time, and therefore kept under the same experimental conditions, the one treated with insulin and ganglioplegics reached temperatures of some degrees lower than the control animal treated with ganglioplegics only.

(2) The animals cooled after having been treated with insulin and ganglioplegics never showed tremor or shivering, in contrast to what was seen in those treated with ganglioplegics only.

(3) The temperature of the animals treated with insulin and ganglioplegics reached lower levels, and for a longer period of time, than that of the controls, the heating being also more rapid after the administration of glucose.

(4) Although the animals cooled with insulin had very low blood sugar, hypoglycaemic convulsions were never noticed below 28°C.

(5) The animals treated with insulin and ganglioplegics never showed shock after hibernation. The awakening was always very rapid at a body temperature of 29–34°C for rabbits, and of 34–36°C for dogs. Even before reaching the normal temperature, the animals took food eagerly and walked spontaneously. A few hours after the hibernation it was hard to recognize the animals hibernated with insulin and ganglioplegics from those that had not undergone any experiment.

Such results, even though briefly described, seem sufficient to show the importance of insulin in the experimental hypothermia. It is possible that combining insulin with the ganglioplegics may succeed in almost completely abolishing the harm produced by the lowering of the body temperature, by inhibiting the increase of the organic combustions at the level of the individual cells and thus protecting them from that hypermetabolism "a frigore" which is so harmful to them.

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Riassunto

Gli autori hanno studiato la possibilità di facilitare l'ipotermia degli omeotermi mediante l'insulina. Hanno osservato che gli animali ibernati in ipoglicemia insulinica non presentano mai chok post-perfrigerazione, che il risveglio è sempre molto rapido e che l'ibernazione ha un decorso molto più soddisfacente dei controlli non trattati con insulina.

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