

Polish Academy of Sciences, Warsaw, Poland.
Institute of Experimental Pathology (Director: L. Paszkiewicz).

THE EFFECT OF ELECTRIC STIMULATION OF THE BRAIN ON ANAPHYLACTIC SHOCK IN GUINEA-PIG

By

W. KARCZEWSKI

In 1955 we have described the phenomenon of the protective effect of electric stimulation of the brain on histamine shock in guinea-pig (9).

After further investigations have been carried out on the behavior of isolated bronchi (11, 12), the cardiovascular reactions and respiratory functions (7, 8, 10, 15) we have concluded that protective effect of brain stimulation consists in a decrease of the susceptibility of bronchial muscles to the bronchoconstricting action of histamine. Therefore it would be a change of the tissue-substrate reactivity induced by an indirect action of a physical factor—in that case electric current. The acceptance of such hypothesis enables to believe that the effect of stimulation could be a repetitious one, that it would happen also in other body reactions which are known to have as a main component a contraction of the smooth muscles. As a model of such reaction anaphylactic shock has been chosen. Without interfering with the permanent dispute concerning the mechanism of the anaphylactic shock and substances being released during the anaphylactic reaction, it is a well known fact that symptoms of the anaphylactic as well as histamine shocks are in guinea-pig quite similar. The last link in both anaphylactic and histamine reactions is a long-lasting bronchospasm leading to death from suffocation.

This obvious similarity seemed to be suitable from the viewpoint of methods to be employed as well as interpretation of obtained results.

MATERIALS AND METHODS

The data presented here were collected from 180 guinea-pigs of both sexes, weighing between 300 and 450 g. Animals were sensitized¹ according to the method described by Herberts (5). That method gave in our experimental conditions an average control mortality of 76 %. After 21 days the experimental animals has been subjected to an electric stimulation of the brain according to a method earlier described (10). Blood pressure and respiration has been recorded by means of a conventional kymographic technique. After 10 minutes of the stimulation intravenous reinjection of the antigen has been made and (in the I-st experimental group) the current has been switched off. In the II-nd and and III-rd experimental groups stimulation has been continued respectively over a period of 30 and 90 sec after the reinjection. Control animals have been reinjected with antigen without prior electric stimulation.

RESULTS

Detailed results are presented in the table I. As will be seen the mortality of animals shows a distinct decrease in the III-rd experimental group. Both I-st and II-nd groups do not show any statistically significant difference in comparison with the control group.

TABLE I
The mortality of animals.

	Control group	I-st exp. group	II-nd exp. group	III-rd exp. group
Total number of animals	64	63	27	26
Mortalitet (per cent)	76	60	63	27

¹ Ovalbumine crist. Sawyer, England.

Thus, the results can be divided into two groups: control, I-st experimental and II-nd experimental groups on one hand and III-rd experimental group on the other. It gives evidence, that a certain threshold exists which can be transgressed when the stimulation is protracted over a definite period after the reinjection. Does it mean that stimulation exerts no influence upon the course of anaphylactic shock in the remaining experimental groups? As can be seen from the statistical calculation concerning the mean time of survival in the animals died, that is not the case (table II).

TABLE II
The mean time of survival with standard error of the mean.
Significance level = 0.05.

	Control group	I-st exp. group	II-nd exp. group	III-d exp. group
Total number of animals died	49	38	17	7
The mean time of survival (sec.)...	237 ± 1	337 ± 1	340 ± 1	317 ± 1

The results indicate in all experimental groups that the mean time of survival is prolonged in comparison with the control group. Anaphylactic shock was in the control animals quite typical and led to death in an average time of 237 sec (Fig. 1). These experimental animals, in which anaphylactic shock resulted at last in a fatal decrease survived an average time between 317–340. Therefore the results produce again two groups but in another arrangement. (Fig. 2). The difference between these two groups is statistically significant. The animals surviving shock after prior electric stimulation showed only transient symptoms of anaphylactic reaction (Fig. 3).

DISCUSSION

The role of the physical factors as reducers of the anaphylactic reaction has been investigated by numerous authors mainly in a relation to the changes in the body temperature. (1, 2, 8, 14, 17, 18). The majority of these authors suggests,

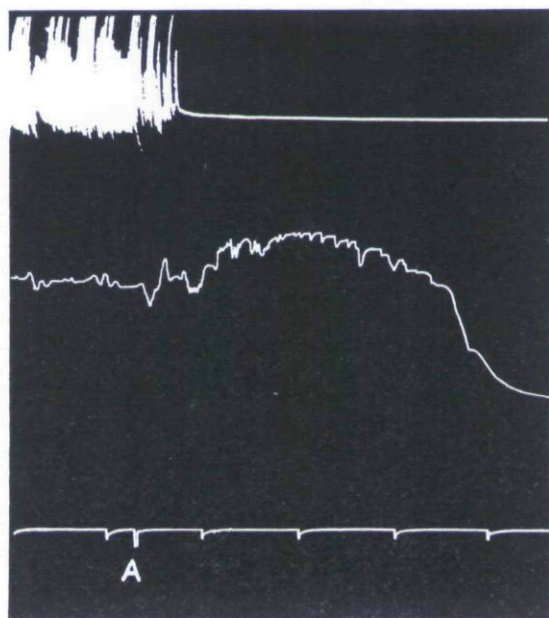


Fig. 1.

Control animal. Curves, from top to bottom: respiration, blood pressure, time marker—1 minute, A—reinjection of the antigen.

that hypothermia decreases the liberation of histamine in the course of antigen—antibody reaction, acting simultaneously on the smooth muscles. According to Mongar & Schild (15) the most effective inhibitors on the anaphylactic reaction are these, which act on last link of the chain of events— i.e. smooth muscles' contraction. As to the effect of other physical factors on the anaphylactic reaction, Toussain (19), has found the electronarcosis to be unable to inhibit the anaphylactic shock. The electric stimulation of the brain employed in our experiments induces a narcosis—like effect; the tone of the muscles and susceptibility to pain stimuli were lowered, the rate of respiration was distinctly diminished. Thus, the observation of Toussain cannot be confirmed, probably due to the different values of the electric current used in our investigations and in those of Toussain.

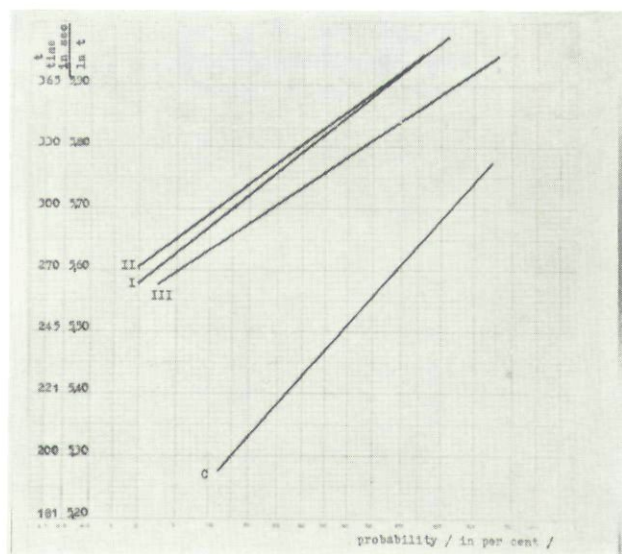


Fig. 2.
Probability of the death in a given time-period.

As it has already been said in both histamine and anaphylactic shocks the protective effect of brain stimulation expresses itself in a diminution of the characteristic bronchoconstriction produced by histamine or products of the antigen—antibody reaction. It is in our opinion due to the change in the reactivity of the bronchial muscles.

This statement is to be confirmed by the results of experiments carried out on isolated lungs and on vagotomized animals (11, 12). It has been shown that the lungs received from stimulated animals react much weaker than those of controls, when histamine or ACh is added to the perfusate.

This effect has an average duration of 10 minutes. Thereafter the reaction of isolated muscles of experimental animals does not differ from that of controls.

On the other hand vagotomy made between the stimulation and histamine injection does not change the protective effect of the stimulation; this effect is however abolished when vagotomy precedes the stimulation.

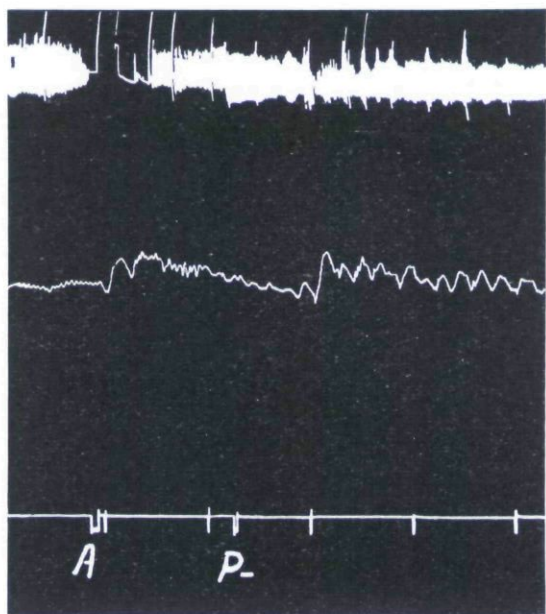


Fig. 3.

Experimental animal. Designation of the curves as above. A = reinjection of the antigen, P- the current switched off.

The physiological tone of the bronchial muscles depends principally upon a selfregulation of them (6) but the vegetative nervous system exerts on it a very great influence. It is known for a long time, that vagi, when stimulated, are able to contract the bronchial muscles, and that vagotomy diminishes the contractibility of them (4, 19).

It is possible to suppose that electric stimulation of the brain as a whole, causes an inhibition of parasympathetic centres and that this inhibition results in a "physiological vagotomy". Such supposition could explain the transientness of the phenomenon, its distinct relation with the factor of time.

The observation of Filip & Szentiványi (3) who have obtained a protection against anaphylactic shock as a result of a damage of the parasympathetic centres of hypothalamus may confirm such supposition. The fact that the stimulation

must be (in the anaphylactic shock) protracted over a definite period after the reinjection when protective effect is to be obtained, indicates some latency in the liberation of the products of the antigen—antibody reaction. The prolongation of the survival time in all experimental groups is not clear; it is due perhaps to some changes in the muscles themselves.

These changes would be however insufficient in the I-st and II-nd experimental groups to protect the animals against death.

Thus it could be supposed that the electric stimulation of the brain inducing a refractory state of the vagi decreases consequently the ability of smooth muscles to contract under the influence of some bronchoconstricting substances.

That hypothesis requests experimental confirmation by means of electrophysiological methods. Adequate experiments are meanwhile performed.

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SUMMARY

The effect of the brain stimulation by electric current has been investigated on the anaphylactic shock in guinea-pig.

The experimental animals have been divided into three groups depending on the stimulation period. The decrease of mortality to 27 per cent has been observed in the group in which the stimulation has been protracted over a period of 90 sec after the reinjection of antigen. In two other experimental groups no significant difference has been observed in the comparison with the control group.

In all experimental groups however, the mean time of survival has been significantly prolonged in comparison with that of the controls. The probable mechanisms of described phenomena are discussed.

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