IMPULSES IN THE SENSORY NERVES IN RESPONSE TO STIMULATION OF THE SKIN RECEPTORS OF IMMUNIZED ANIMALS WITH ANTIGEN

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We showed in a previous paper [1] that the intradermal injection of antigen causes stimulation of receptors, accompanied by a characteristic flow of impulses along a sensory nerve.

We know that the immunized animal reacts differently from the unimmunized by the production of antibodies in response to a repeated injection of antigen. On repeated injection of antigen into immunized animals a rapid and high increase in the antibody titer takes place. In unimmunized animals the injection of the same dose of antigen usually causes a slow and slight increase in the antibody titer.

Believing that the production of antibodies has a reflex mechanism, and that the impulses in the nerve may be one of the factors responsible for the formation of antibodies, we attempted to study the reaction of a sensory nerve of an immunized animal to the intradermal injection of antigen.

EXPERIMENTAL METHOD

Experiments were carried out on dogs immunized by triple injection of typhoid vaccine. The animals took part in the experiment 7-10 days after injection of the last dose of vaccine.

The flow of impulses in sensory nerves (auricular and saphenous nerves) was studied before and after the intradermal injection of typhoid antigen into the region innervated by the corresponding nerve.

In control experiments dysentery antigen was injected. The nerve to be examined was placed on a recording platinum electrode (distance between electrodes 4 mm), the potentials were fed into an amplifier (type 2-cube-2) and recorded on a loop oscillograph.

After the initial flow of impulses had been recorded the antigen was injected and the changes in the flow of impulses recorded immediately after the injection or 1, 3 and 5 minutes later.

EXPERIMENTAL RESULTS

In 17 dogs immunized with typhoid vaccine it was shown that the intradermal injection of typhoid bacillus antigen caused a significantly greater reaction than in unimmunized animals.

Two types of reaction were observed. In the first case, intradermal injection of typhoid bacillus antigen caused a slow change of the bioelectric potentials. The electroneurogram showed the appearance of separate, biphasic spike oscillations, after which the frequency of the potential variations increased and sometimes acquired the character of grouped impulses.

As a rule after 15-20 minutes the bioelectrical activity of the nerve increased sharply and changed into

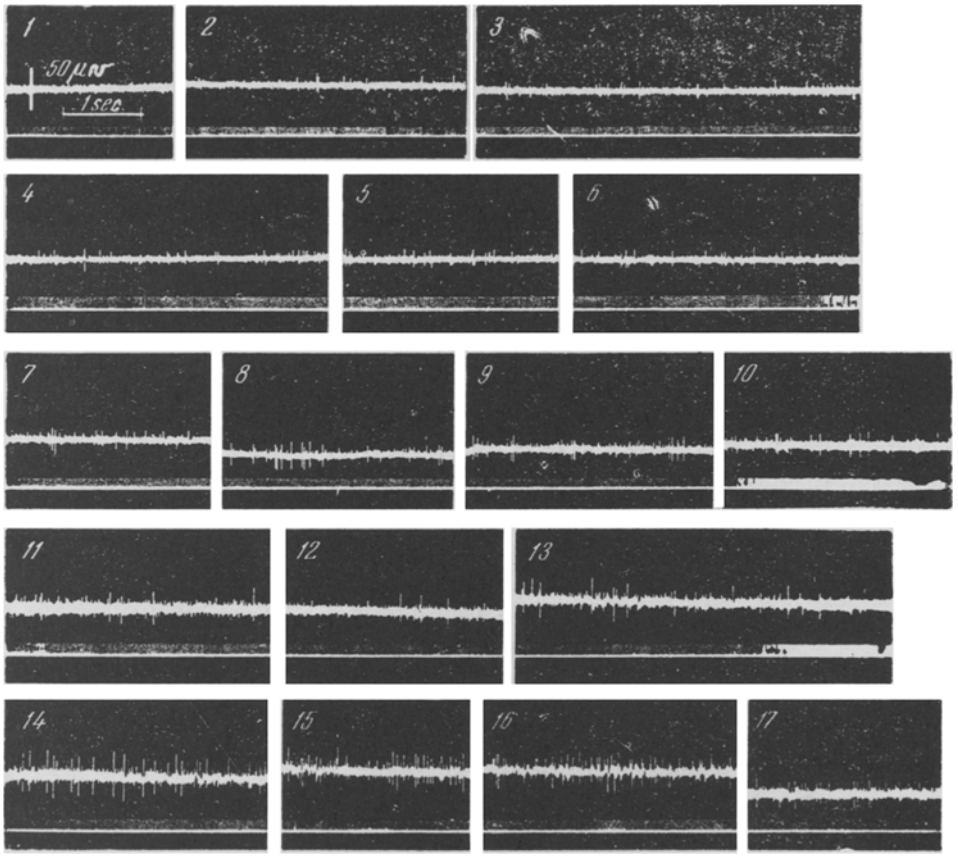

Fig. 1. Changes in the action potentials of the saphenous nerve of an immunized dog after intradermal injection of typhoid bacillus antigen (first type of reaction). Tracing 1) initial flow of impulses; 2-17) tracing made after 30 seconds, and 1, 3, 5, 7, 10, 15, 17, 20, 25, 30, 35, 40, 50, 60 and 75 minutes respectively after injection of antigen.

a continuous flow of impulses. This reaction was comparatively prolonged and was recorded for 70-80 minutes.

In unimmunized animals the same vaccine caused an identical flow of impulses but the reaction did not last longer than 7-8 minutes.

In the electroneurograms of experiment No. 6 (Figure 1), by comparison with the initial flow of impulses [1], changes were seen, which were not most pronounced 10 minutes [7] after injection of the antigen and which lasted for an hour [8-16].

The intradermal injection of typhoid antigen into immunized animals thus caused a more prolonged reaction than took place in the unimmunized animals.

In the second case, immediately after the injection of typhoid antigen, the immunized animals developed a well-marked flow of impulses, although the duration of this reaction was considerably less than in the first group of animals.

In Fig. 2 are shown extracts of electroneurograms recorded before and 1, 3, and 5 minutes after injection of the antigen, from which it can be seen that changes in the initial activity [1] developed immediately after injection of the antigen, and the excitation which ensued continued to be recorded for 15 minutes [7].

Both types of reaction were characterized by a more prolonged flow of impulses than occurred during the changes in bioelectrical activity of the same sensory nerves in response to injection of the same antigen into intact animals.

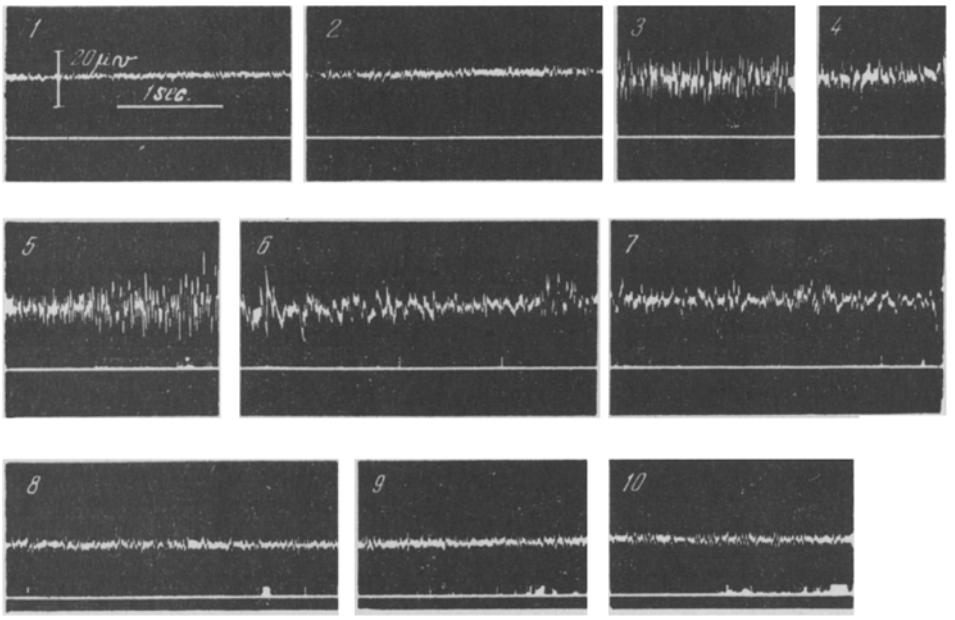

Fig. 2. Changes in the action potentials of the saphenous nerve after intradermal injection of typhoid antigen (second type of reaction).
Tracing 1) initial flow of impulses; tracing 2-10) made 30 seconds and 1, 3, 5, 10, 15, 17, 20 and 25 minutes respectively after injection of the antigen.

The high intensity and the long duration of the reaction was probably one cause of the more intensive production of antibodies in the immunized than the unimmunized animals.

Preliminary immunization of the animals evidently increased the excitation of the receptors toward the corresponding antigens, so that they caused a more intensive stimulation. The strong stimulation of the receptors

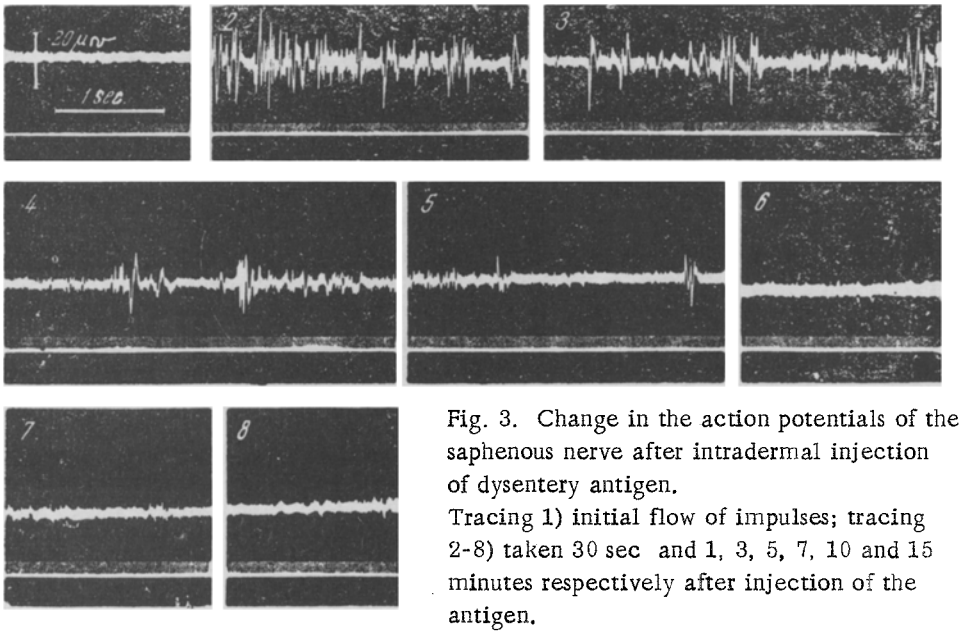

Fig. 3. Change in the action potentials of the saphenous nerve after intradermal injection of dysentery antigen.
Tracing 1) initial flow of impulses; tracing 2-8) taken 30 sec and 1, 3, 5, 7, 10 and 15 minutes respectively after injection of the antigen.

and the weaker adaptation of the receptors towards the antigen were responsible for the intensive production of antibodies in the immunized animals. The increase in this reaction demonstrated that the adaptation of the animal

proceeded along the lines of intensification of the reaction of the nervous reflex apparatus to antigenic stimulation.

The question arose: to what extent was this reaction specific?

In order to answer this question, control experiments were set up. Dogs were immunized with typhoid vaccine and given injections of dysentery bacilli, after which an ordinary reaction was observed in the sensory nerve, whose duration did not exceed the limits which we had found in unimmunized animals [1]. The reaction lasted as a rule for 5-7 minutes (Fig. 3).

It can be seen in this figure that in response to injection of dysentery antigen, the characteristics of amplitude and frequency of the reaction differed from those observed in the main experiments (see Figs. 1 and 2). It must be pointed out that this reaction was similar in its nature to that observed in the unimmunized animals.

The data given demonstrate that in the process of immunization of animals a change occurs in the specific sensitivity of the receptor apparatus of the skin. The skin receptors of immunized animals react for a longer period of time to specific antigens.

This intensification of the reaction is probably one of the more important factors determining the changed reaction of immunized animals to injection of antigen.

The change in the reaction demonstrates once again the an immunogenesis is brought about primarily by stimulation of the nervous system and of its receptor apparatus.

It may be thought that in the process of immunization changes occur in the reactivity not only of the skin receptors but also of other components of the reflex apparatus. A study of the functional changes in the other links of the reflex apparatus during immunization is of great interest and will be the subject of our later research.

SUMMARY

The skin receptors of the immunized animals react to specific antigens for a more prolonged time and often with greater intensity. The reaction is more prolonged, the frequency of the bioelectrical potential oscillations of the sensory nerves becomes greater. This is, probably, one of the most important factors showing the changed reaction of the immunized animals to the administration of the antigen.

LITERATURE CITED

[1] A. N. Gordienko, V. I. Kiseleva, B. A. Saakov et al., Byull. Éksptl. Biol. i Med., Supplement to No. 1, 147-151 (1957).