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THE ELECTRICAL ACTIVITY OF THE VAGUS NERVE IN ANAPHYLACTIC SHOCK

By

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We have earlier described the protective effect of an electric stimulation of the brain in histamine (8, 12, 13) and anaphylactic shock (9) in guinea-pig.

The results of the investigations showed that the striking diminution in the mortality of animals stimulated before the shock was induced, depends upon inability of bronchial musculature to develop the characteristic strong and prolonged contraction after histamine or antigen - antibody reaction products came into contact with the tissue of lungs (9, 14). It was possible to suppose that the effect of the stimulation consists in an inhibition of the brain parasympathetic centres and in consequence of the motor functions of the vagus nerve.

It is well known that the afferent and efferent fibres of the vagus play an important part in the mechanism of bronchospasm. The afferent fibres transfer information from pulmonary stretch receptors which signalize changes in the degree of the distention of lungs (1). The efferent, motor fibres to the lung are probably bronchoconstrictor; there is evidence that stimulation of the peripheral stump of the vagus results in a bronchoconstriction (4, 16) and that vagotomy or atropine administration prevent the constriction of bronchi (14). Recently, Widdicombe investigated single efferent vagal fibres to the lungs of the cat and showed that these fibres could actually be bronchoconstrictor. Moreover, the author concluded that "there is a reflex bronchoconstriction in response to irritant stimuli and asphyxia" (17).

The task of the present work is to prove whether the events occurring during anaphylactic shock in guinea-pig in its shock organ, i.e., lungs could be explained on the basis of an analysis of the electrical activity in the peripheral and central stumps of the vagus nerve.

The following papers will attempt to answer the question to what extent the protective effect of the stimulation of the brain could depend upon modifications in the activity of the parasympathetic system.

METHODS

All investigations were performed on unanaesthetized guinea-pigs of both sexes, weighing from 300 to 500 g. The results were collected from 60 experiments.

Anaphylactic shock was produced in the manner described by *Herberts* (7).

Electrical activities of the vagus nerve were studied in the following way:

The animals were thoroughly restrained on a warmed operation table. A length of about 40 mm of a cervical vagus was carefully prepared and desheated under a binocular magnifying glass. In animals in which the efferent activity was to be studied the nerve was cut near the level of the clavicle. In another group in which the afferent activity was examined the nerve was cut near the level of the thyroid cartilage. In all the investigations the right vagus was used and the left remained intact, although no detectable differences between the activity of both nerves were observed in the course of pilot experiments. The nerve was mounted on the recording electrode consisting of a pair of silver-silver chloride or platinum wires connected with the input of a differential A.C. amplifier. The earthing electrode was mounted closely to the recording one in such a way that it covered the adjacent muscles of the neck; this eliminated the influence of strange electric fields on the vagal activities. The signals were displayed on a dual-beam oscilloscope and photographed on film. One beam was used to record the action potentials, the second one to pick-up the respiration rate. For this purpose a resistance gauge designed at this Institute was mounted closely to the animal's mouth and connected with the amplifier. The recording started about five minutes before the reinjection of the antigen (control activity) and was then continued in the course of the shock. The experiment was completed by a blockade of nerve transmission. This was performed by placing one droplet of 2 per cent Xylocaine on the nerve trunk at a distance of about 4 mm from the recording electrode in order to prove

¹ Alvar-Reega VIII.

² Cossor 1035 MK II A, Cossor Camera 1428.

³ Xylocaine-Astra, Sweden.

whether the electrical phenomena occurring in anaphylactic shock are not influenced by muscular or other activities. The photographic material obtained was examined under a tenfold magnification. Both the frequency and amplitude of impulses were taken into account. A weakness of this method is that no precise data concerning the frequency of spikes can be obtained because of a distinct superimposition. Also the activities of non-pulmonary fibres cannot be separated. These problems are now under investigation and the results will be reported later.

RESULTS

Control afferent activity:

The pattern of the afferent activity was very characteristic. It was composed of periodic bursts locked to the inspiratory phase of the respiratory cycle. The impulses started to fire simultaneously with the beginning of inspiration, the number of spikes increased progressively reaching its maximum at the peak of inspiration. Expiration was accompanied by a short gradual decrease in the frequency of impulses. It should be stressed that the changes in the whole nerve pertain not only to the frequency but also to the amplitude of impulses. The later progressively increased during the inspiration and decreased during the expiratory phase. The whole respiratory cycle of activity was therefore spindle-shaped. The interval between expiration and inspiration, thus the inactive phase, was in most cases composed of low-voltage potentials sometimes hardly distinguishable from the noise level (fig. 1 A).

Afferent activity in the anaphylactic shock:

Immediately after the antigen had been reinjected, the afferent activity of the vagus changed entirely. The periodic bursts disappeared (simultaneously with the cessation of breathing), the average frequency and amplitude of impulses significantly grew. The electrical activity was in consequence composed of high-voltage spikes whose amplitude was higher than the maximal amplitude of potentials at the peak of inspiration (fig. 1 B).

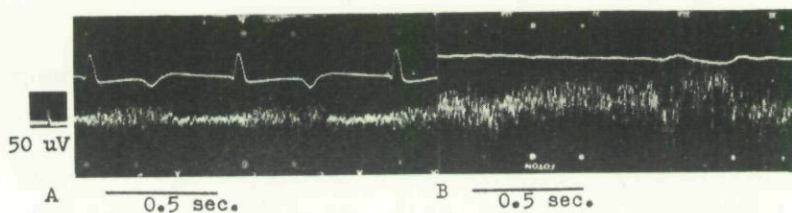


Fig. 1.

Afferent activity of the vagus nerve before, and in the course of anaphylactic shock. Upper traces: respiration (upwards: beginning of inspiration; downwards: expiration), lower traces: electrical activity of the nerve. A: control picture. B: same animal, 30 sec. after reinjection of antigen. Arrest of respiration, marked increase in the electrical activity of the nerve.

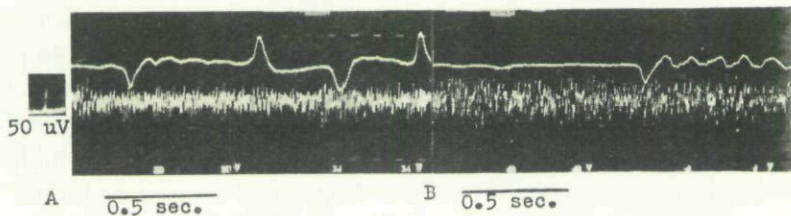


Fig. 2.

Efferent activity of the vagus nerve before, and in the course of anaphylactic shock. Traces as in Fig. 1. A: control picture. B: same animal 30 sec. after reinjection of antigen. Arrest of respiration, marked increase in the electrical activity of the nerve.

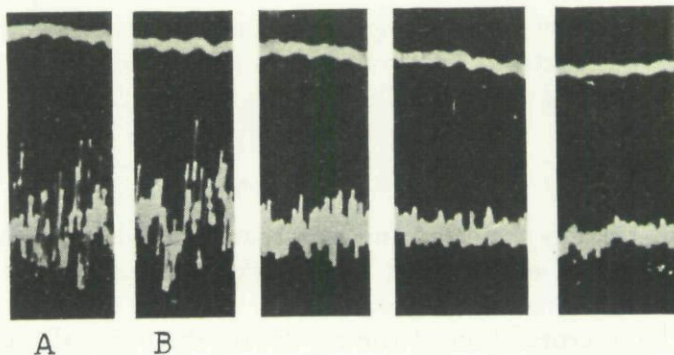


Fig. 3.

Electrical activity of the vagus nerve (efferent stump) in anaphylactic shock before and after blockade of transmission. Traces as in Fig. 1. Between A and B one droplet of Xylocaine was placed on the nerve. Next photographs made 30, 60, and 90 sec. later. Complete disappearance of all action potentials.

Control efferent activity:

The spontaneous activity recorded from the central stump of the vagus nerve was composed of impulses that formed no characteristic sequences; only occasionally one observed short volleys of action potentials that appeared just before the end of inspiration and just before the end of the expiratory phase. In general, however, the activity was entirely irregular (fig. 2 A).

Efferent activity in the anaphylactic shock:

The electrical activity observed in the central stump of the vagus in the course of anaphylactic shock exhibited similar changes as those described for the afferent activity. The symptoms of developing anaphylactic shock (first of all dyspnoea) were accompanied by a violent increase in both frequency and amplitude of impulses. The activity was composed of high-voltage spikes and could not be distinguished from the afferent activity in the course of shock (fig. 2 B). Such a picture was maintained for about 10 minutes after the death of the animal, then the activity progressively disappeared.

Xylocaine test:

One droplet of xylocaine placed on the nerve close to the recording electrode brought about a rapid and complete disappearance of all electrical discharges (fig. 3).

DISCUSSION

The results reported indicate that anaphylactic shock in guinea-pig is accompanied by a marked increase in the electrical activity of the vagus nerve.

The interpretation of the results on the basis of view accepted by some authors (5) that in anaphylactic shock there is a general increase in the parasympathetic tone seems to be insufficient to explain the mechanism that underlie the anaphylactic reaction occurring in the shock organs.

Constriction of bronchi and, in consequence, asphyxia are the most conspicuous symptoms of anaphylactic shock in the guinea-pig. At the same time, the guinea-pig is an animal in which the vagal proprioceptive control of respiration is particularly important (15). It could therefore be expected that severe dyspnoeic disturbances, typical for anaphylactic shock in this animal should modify the normal pattern of the electrical activity of the vagus nerve. The pulmonary stretch receptors signalize changes in the physical state of lungs (1). Bronchoconstriction brought about by an inhalation of histamine aerosol enhances the activity of stretch receptors in cats and rabbits (18). A marked increase in the electrical activity in the peripheral stump of the vagus, as observed in anaphylactic shock could therefore be attributed mainly to a stimulation of a large number of stretch receptors in the lungs. On the other hand, the secondary changes in the systemic blood pressure could also be responsible for the sensitization of pulmonary stretch receptors (2, 11). However, in anaphylactic shock in the guinea-pig the afferent vagal activity clearly reflected the respiratory alterations while no corresponding changes were brought about by the initial, almost twofold rise and the subsequent fall of the blood pressure to zero.

The interpretation of events occurring in the central stump of the vagus nerve presents serious difficulties. The physiological function, electrophysiological pattern, central nervous origin of the efferent vagal activity in the guinea-pig (and to a less degree also in other animals) are still surprisingly obscure. It is evident that at least some groups of the efferent fibres are stimulated by asphyxia and strong inflation. Moreover, one can assume the existence of a reflex stimulation of motor nuclei of the vagus in response to irritant stimuli and asphyxia (17). All these elements are distinctly pronounced in anaphylactic shock in guinea-pig. There is no evidence that the increase in the efferent activity of the vagus could originate in the higher nervous structures. Electroencephalographic investigations of *Heimlich et al.* (6) as well as our own unpublished experiments showed that the increase in the EEG

in the course of anaphylactic shock is followed in a few minutes by a depression of the electrical activities. The efferent vagal activity was maintained on the level observed in shock for 10 minutes and more after disappearance of all electroencephalographic waves. This suggests a peripheral rather than central origin of the stimulus. A reflex which begins in the pulmonary stretch receptors and leads to further bronchoconstriction seems to be the most probable explanation of the electrophysiological events on one hand and the irreversibility of the anaphylactic bronchospasm on the other.

The possible influence of the expiratory centre on the motor nuclei of the vagus cannot be excluded. The role of Hering-Breuer inflation reflex is commonly known. The afferent vagal discharges inhibit the inspiratory, and stimulate the expiratory activity of the respiratory centres (19). This effect is particularly distinct in the course of anaphylactic shock; the increased traffic of action potentials from the lungs is probably the cause of the typical strong expiratory efforts of the animal. Thus, the increase in the efferent activity could partially result from the excitation of the expiratory centre. Although the duration of the events observed in the activity of the vagus nerve significantly exceeds that of respiratory movements of the chest and nostrils, such a possibility could be excluded, or confirmed only by means of direct methods; by simultaneous records from efferent vagal fibres and the phrenic nerve, or from the motor nuclei of the vagus and the respiratory centre.

The results described suggest that the increase in the electrical activity of the vagus nerve in the course of anaphylactic shock is strictly related to the anaphylactic reaction of the shock organ. Our results confirm also the view that the motor fibres of the vagus nerve can participate in a reflex bronchoconstriction.

SUMMARY

The electrical activity of the vagus nerve was studied in guinea-pigs in which lethal anaphylactic shock was produced. The experiments were carried out on two groups of animals: in one of them the afferent vagal activity was investigated before, and in the course of anaphylactic shock. In the second group the same observations were made on the efferent activity of the nerve.

It was found that anaphylactic shock entirely changes the electrophysiological pattern of the activity of the vagus nerve. The anaphylactic reaction was accompanied by a marked and prolonged increase in the electrical activity recorded from the central and peripheral stumps of the vagus.

It is concluded that the increase in the afferent activity is directly related to the anaphylactic reaction developing in the shock organ, i.e., to the constriction of bronchi and strong stimulation of pulmonary stretch receptors.

The increase in the activity of efferent, motor fibres could probably be attributed to a reflex stimulation which leads to the further constriction of bronchi. The observations confirm the view that the efferent fibres of the vagus nerve are bronchoconstrictor and that bronchospasm can be induced reflexly in reesponse to irritant stimuli and asphyxia (17).

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