THE TONIC INFLUENCE OF THE LUNG RECEPTORS ON THE RESPIRATORY CENTER AND THE MECHANISM OF DYSPNEA IN LUNG LESIONS

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During his investigations of the activity of single afferent fibers of the vagus nerve in 1933, Adrian [4] found that only the stretch receptors of the lungs take part in normal respiration; impulses arising from these receptors inhibit inspiration. On the basis of these findings, Christie [8] formulated the theory that the increase in the respiration rate in lung lesions arises as a result of an increase in the flow of impulses from the stretch receptors of the lungs, leading to the premature cessation of inspiration. However, direct investigations of the activity of single afferent fibers of the vagus nerve in the presence of a variety of pathological processes in the lungs—congestive hyperemia [7, 10, 11], edema [12, 14], pulmonary embolism [13], pneumonia [3]—have not confirmed this hypothesis. In these conditions the flow of impulses from the stretch receptors of the lungs either was not increased or was increased too little to afford an explanation of the increase in the rate of respiration.

The afferent impulses from the stretch receptors which were studied in these experiments travel along the A-fibers. Histological investigations have shown, however, that the great majority of the fibers of the vagus nerve, including its bronchial branches, are nonmedullated C-fibers [5].

To evaluate the overall activity of the receptors in lung lesions—edema and inflammation—the method of "colliding impulses" [9] was used.

METHOD

Experiments were carried out on 32 cats under anesthesia (urethane in a dose of 250 mg/kg, chloralose in a dose of 50 mg/kg), thoracotomized and maintained on artificial respiration. The right vagus nerve was divided below the ganglion nodosum and the peripheral segment was placed on stimulating electrodes. The nerve was stimulated with rectangular pulses of the duration and strength necessary to produce excitation of the maximal number of fibers of the particular group. The composite action potential was recorded in the part of the nerve situated in the lower part of the neck or the upper part of the thorax. Recordings were made with a Disa three-channel amplifier and a type S1-4 oscillograph. A driven sweep was used. The beam was triggered by an impulse from a stimulator synchronized with the phases of the respiratory cycle. To exclude impulses from other organs both vagus nerves were divided above the diaphragm, and as many as possible of the cardiac branches on the right side were severed. Pulmonary edema was caused by the injection of 0.5 ml of a 40% solution of glucose into each lobe of the lung, and inflammation by injection of 2 ml of hot water into each lobe.

RESULTS AND DISCUSSION

In normal conditions the amplitude of the individual oscillations of the A-wave of the composite action potential of the vagus nerve clearly changed with the phases of respiration. In inspiration their amplitude fell and in expiration it rose (Fig. 1, top). The fall in the amplitude of the A-waves was more marked the more strongly the

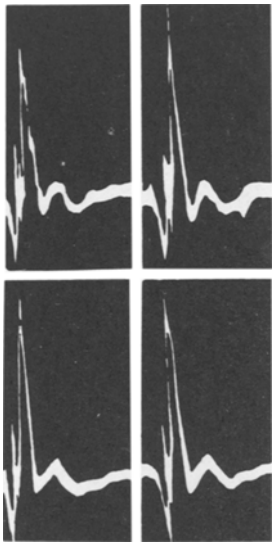

Fig. 1. A-wave of the composite action potential of the vagus nerve. Top) before injury to the lungs; amplitude of A-waves in inspiration (left) is smaller than in expiration (right). Bottom) after the development of edema; amplitude of the A-waves in inspiration (left) has increased and is now the same as in expiration (right). Frequency of stimulation of nerve 1 per sec (in inspiration or in expiration). Each tracing is the result of superposition of 5 sweeps of the beam. Distance between stimulating and recording electrodes 58 mm.

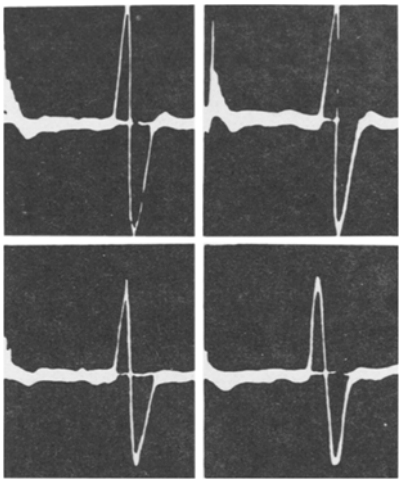

Fig. 2. C-wave of the composite action potential of the vagus nerve. Top) before injury to the lungs; amplitude of A-waves in inspiration (left) is equal to the amplitude of the C-waves in expiration (right). Bottom) after the development of edema. Amplitude of the C-waves has diminished equally in both inspiration (left) and expiration (right). Frequency of stimulation of nerve 1 per sec (in inspiration or in expiration). Each tracing is the result of superposition of 5 sweeps of the beam. Distance between stimulating and recording electrodes 58 mm.

lungs were stretched. This fully concurs with the view that the discharges of impulses from the stretch receptors of the lungs do in fact spread along the thick medullated (group A) fibers. Similar results were obtained by A. V. Zeveke [1].

As the development of the pathological process advanced, 30-40 min after injury to the lung tissue the amplitude of the A-waves in inspiration increased, and often equalled the amplitude of the A-waves in expiration (Fig. 1, bottom). Hence, it follows that when pathological changes are present in the lungs the flow of impulses from the stretch receptors in inspiration not only does not increase but, on the contrary, it actually decreases slightly. This may evidently be accounted for by the fact that in edema and inflammation the degree of stretching of the lungs is reduced.

In contrast to the A-wave of the composite action potential of the vagus nerve, the amplitude of the C-wave in normal conditions did not change with the phases of the respiratory cycle (Fig. 2, top). It remained constant even during extreme inflation and deflation of the lungs. The receptors innervated by these fibers are evidently not mechanoreceptors. Obvious changes in the size of the C-wave appeared only during the development of edema and inflammation. The amplitude of the C-wave diminished, but it remained equal in inspiration and expiration (Fig. 2, bottom). Hence, it follows that in edema and inflammation the flow of impulses spreading from the lung tissue along the C-fibers increased. This flow of impulses was constant and independent of the phases of the respiratory cycle. Inflammation and edema are accompanied by the accumulation of various ions, especially of potassium, in the tissues. In this connection it is interesting to note that intravenous injection of potassium ions causes a depression of the C-wave of the composite action potential of the vagus nerve [2].

The facts described above shed new light on the mechanism of the disturbance of respiration in lung lesions. It was shown comparatively recently that cathodic depolarization causes facilitation of the respiratory neurons [6]. The constant increase in the flow of impulses along the C-fibers of the vagus nerve observed in edema and inflammation of the lungs may possibly have the same depolarizing influence on these neurons. The facilitation of the reactions to the rhythmic volleys from the stretch receptors arising in this manner leads to frequent and shallow respiration characteristic of these diseases.

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