

Polish Academy of Sciences, Medical Research Centre, Laboratory of
Neurophysiology, Dworkowa 3, Warsaw, Poland.

ACTIVITY OF PHRENIC MOTONEURONS IN ANAPHYLACTIC SHOCK IN THE RABBIT

By

MAŁGORZATA SZEREDA-PRZESTASZEWSKA

The vagus and phrenic nerves are the main elements controlling the work of the respiratory apparatus. The explanation of the problem of the neural control of breathing in anaphylactic shock therefore requires not only an examination of the activity of the vagus nerves (16, 17), but also a determination of the contribution of phrenic motoneurons. Similar reactions of vagal and phrenic motoneurons to different stimuli show (4), that both outputs of "respiratory centres" controlling the work of the respiratory apparatus are subordinated to the same higher centres. It might be supposed, that the constriction of airway smooth muscles in anaphylactic shock would be followed by changes in phrenic nerve activity. The latter aiming to adjust the work of the diaphragm to increased resistance in the airways. The activity of the phrenic nerve is proportional to the level of total nervous discharges of respiratory "centres" and to the tidal volume (2, 13). It increases linearly with the increase of tidal volume and the same applies to the electromyogram of the diaphragm (8). The phrenic nerve controls the diaphragm—the strongest inspiratory muscle, which is responsible for about 75 per cent of the effective respiration (14).

It seemed important to investigate the pathway of information for the phrenic nerve in anaphylactic shock. In light of the data quoted it is possible to suppose that the changes of respiration observed in anaphylactic shock and particularly the increase in resistances to flow—would cause an increase

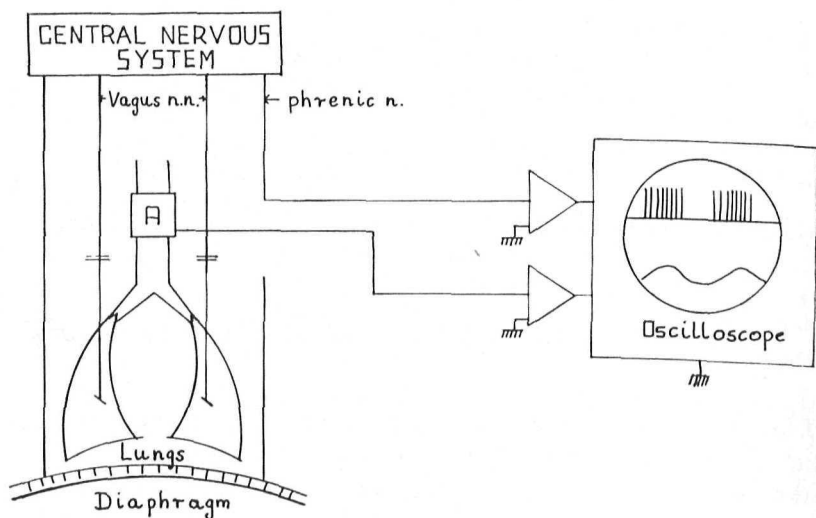


Fig. 1.

Scheme of recording. A: respiratory resistance gauge.
The line across the drawing of the vagus indicate vagotomy.

in phrenic nerve activity corresponding to the increase of the diaphragmatic electromyogram in guinea-pig anaphylaxis (9), and to the increase in the activity of vagal motoneurons in rabbit anaphylactic shock (17).

MATERIAL AND METHODS

The experiments were made with 36 male rabbits, breathing spontaneously and artificially ventilated either with intact vagus nerves or unilaterally and bilaterally vagotomized. Methods of preparing the nerve fibres, recordings and the way of sensitization of animals have been described elsewhere (15, 16). A scheme of recordings is given in Fig. 1.

WORKING OUT OF RESULTS

In oscillographic changes in respiratory rate and in bio-electrical activity of phrenic motoneurons were estimated. According to Gill (5) the following designations for obtained parameters were introduced:

- τ – number of breaths per minute (frequency of breathing),
- T – duration of one phrenic volley (active phase),
- N – number of impulses in one volley,
- f – mean frequency of impulses in one volley,
- SP – expiratory pause (inactive phase).

The mean of the parameters mentioned above, determining the pattern of the bioelectric activity of the investigated motoneuron, were calculated in absolute values. The control values showed some dispersion possibly caused by the kind of fibres innervating different parts of the diaphragm (11). The final calculations were presented in relative values. The values of all parameters obtained after antigen administration were divided by control values. The control value of each parameter thus being 1, all results above and below unity illustrate appreciable increase or decrease of the parameter. The mean values were obtained from all parameters in relative figures in the given experimental groups and served as data to diagrams. For every parameter a separate diagram was drawn. On the abscissa is indicated the time (1–10 min.) after antigen administration, on the ordinate the relative values (1 as a control value).

RESULTS

1. *Changes in the Activity of Phrenic Motoneurons in Animals with Intact Vagus Nerves*

a. *Animals Breathing Spontaneously*

Increase in respiratory frequency was associated with a decrease of duration of the volleys and shortening of the inactive phase. A characteristic feature in this group was the appearance of tonic (frequency-modulated) activity. This type of change was always observed in association with great acceleration of respiratory rhythm. The transition of phasic to tonic activity was accompanied by an increase in mean frequency of impulses. This type of activity lasted several

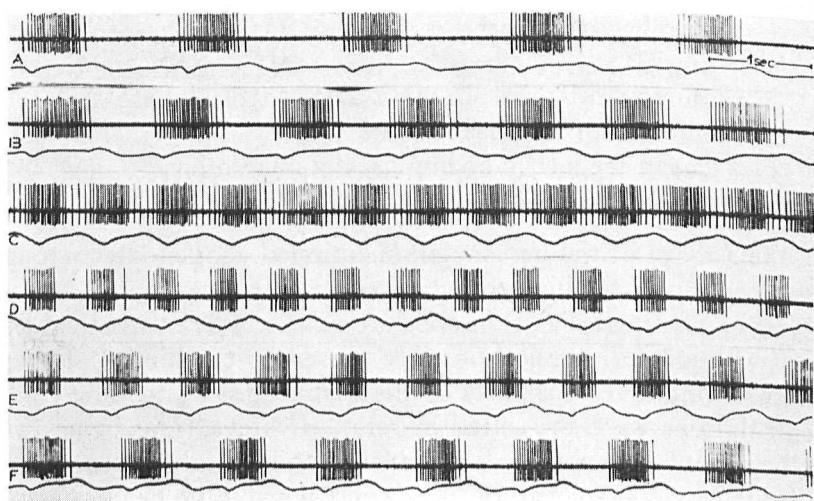


Fig. 2.

Changes in phrenic motoneuron activity in anaphylactic shock. Animal breathing spontaneously, vagus nerves intact. Upper tracing: activity of phrenic motoneuron. Lower tracing: respiration curve. Downward deflection: inspiration. A: control record, B: 1 min., C: 2 min., D: 4 min., E: 9 min., F: 12 min. after antigen administration. Spike potentials retouched.

minutes, whereupon the phasic activity returned. The type of reaction is shown in Fig. 2.

b. *Animals Artificially Ventilated*

In animals artificially ventilated the frequency of phrenic volleys remained stable. The characteristic feature was an increase in the duration of phrenic volleys on the cost of a shortening of the inactive phase. It was accompanied by an increase in number and mean frequency of impulses. This reaction is illustrated in Fig. 3.

2. *Changes in the Activity of Phrenic Motoneurons in Animals with one Vagus Nerve Cut*

The results of this subgroup are shown in Fig. 4. In the course of anaphylactic shock, the respiratory rhythm does not

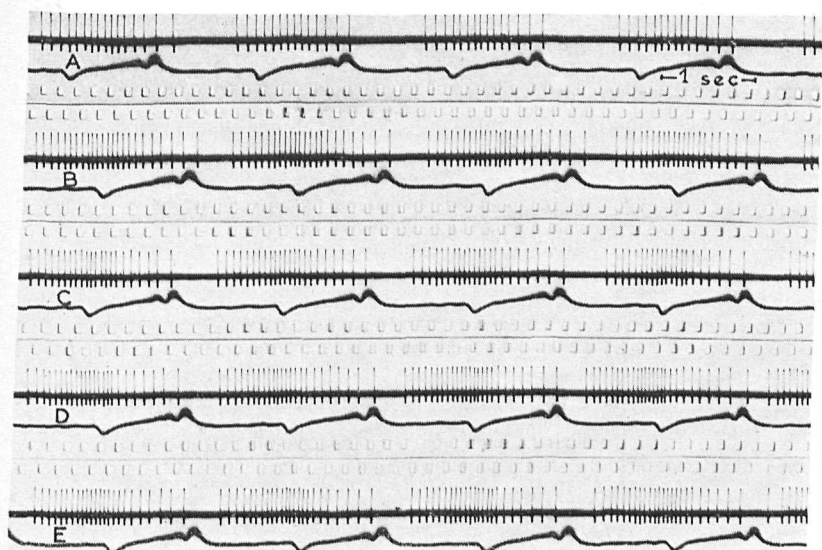


Fig. 3.

Changes in phrenic motoneuron activity in anaphylactic shock. Animal artificially ventilated, vagus nerves intact. Lower tracing: respiratory pump rhythm. A: control record, B: 1 min., C: 1 min. 30 sek., D: 2 min. 30 sek., E: 3 min. after antigen administration.

accelerate significantly. The peak of acceleration appears within 1–4 min. of the anaphylactic shock, whereupon the respiration slows down, reaching nearly the control values. The duration of volleys (T) decreases parallel to the increase in breathing frequency persisting below the control values to the end of the observation. The decrease in the number of impulses (N) is slight, which may explain a relatively great increase in the mean frequency of impulses. The shortening of the inactive phase is associated with maximal acceleration of respiratory rhythm and nearly reaches the control values at the end of the observation. A typical experiment is shown in Fig. 5.

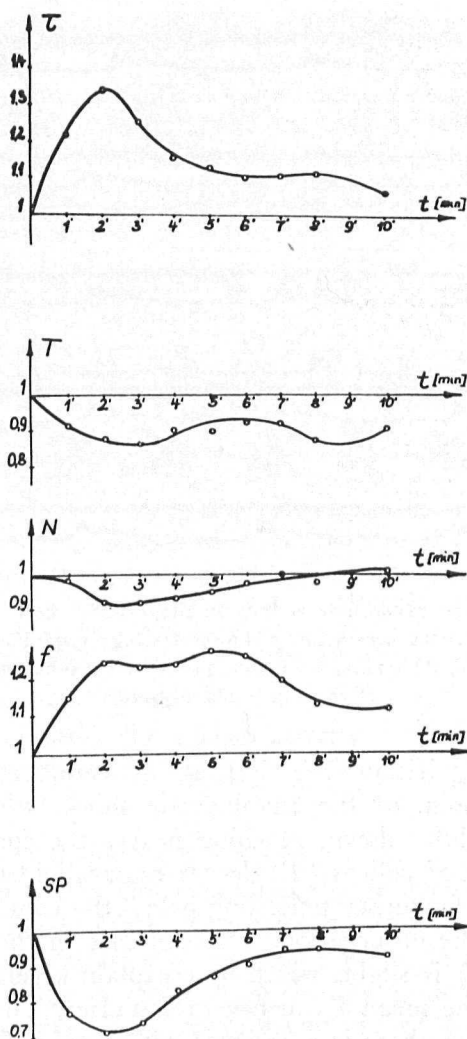


Fig. 4.

Diagram of reaction of phrenic motoneurons of unilaterally vagotomized, spontaneously breathing animals. τ : frequency of breathing, T : duration of volley, N : number of impulses in one volley, f : mean frequency of impulses in one volley, SP : expiratory pause (silent period).

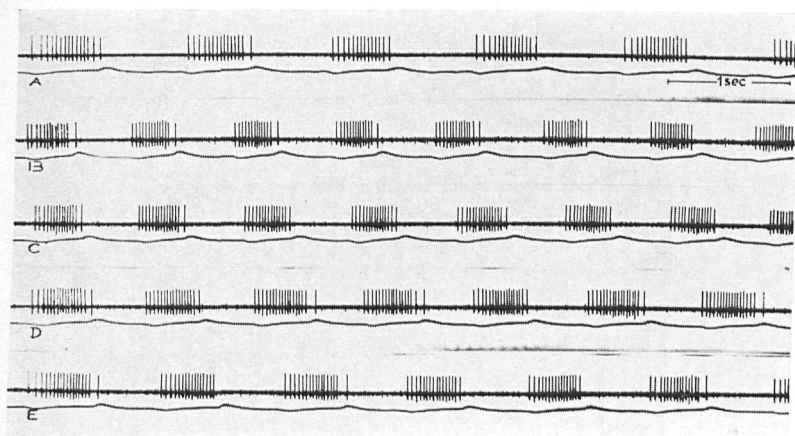


Fig. 5.

Changes in phrenic motoneuron activity in anaphylactic shock. Animal breathing spontaneously with one vagus nerve cut. A: control record, B: 1 min., C: 2 min., D: 3 min., E: 7 min. after antigen administration. Spike potentials retouched.

3. *Changes in the Activity of Phrenic Motoneurons in vagotomized Animals*

a. *Animals Breathing Spontaneously*

The results in this subgroup are graphically presented in Fig. 6. The acceleration of respiratory rhythm is of lesser degree than in subgroup 2. The peak of this acceleration appears slightly later, between 2–5 min. of the shock. All the parameters show changes directed as in group 2. The increase in the mean frequency of impulses is less pronounced than before vagotomy. A typical experiment of this group is shown in Fig. 7.

b. *Animals Artificially Ventilated*

The results are shown in Fig. 8. The acceleration of volleys appear in the second minute of shock, reach the peak between 3–5 min. and return to the control values. Simultaneously with the acceleration the duration of the volleys decrease (T) and the number of impulses (N) becomes slightly lower and

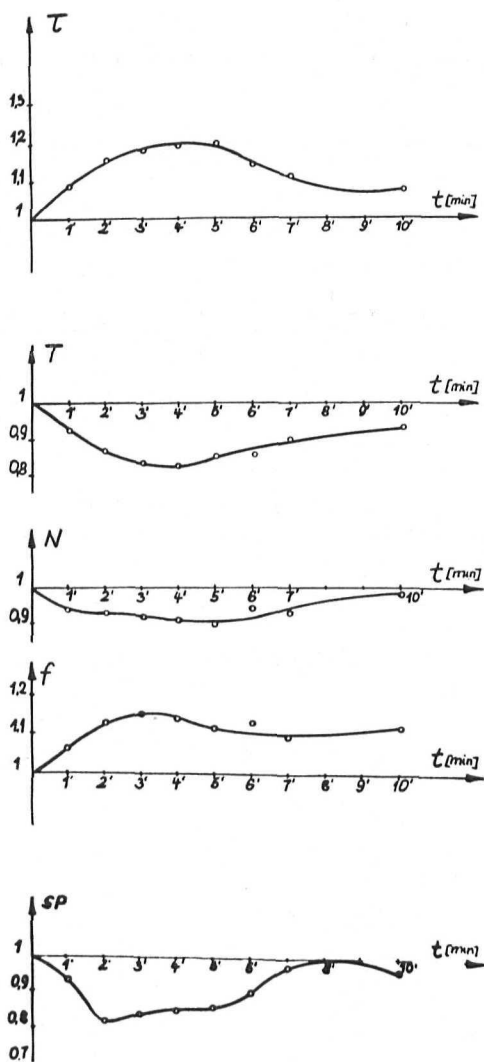


Fig. 6.

Diagram of reaction of phrenic motoneurons in vagotomized, spontaneously breathing animals.

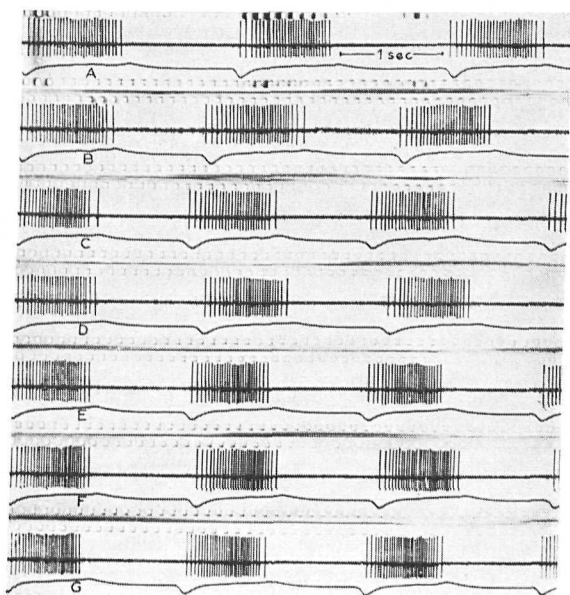


Fig. 7.

Changes in phrenic motoneuron activity in anaphylactic shock. Animal breathing spontaneously, both vagus nerves cut. A: control record 10 min. after bilateral vagotomy, B: 1 min., C: 2 min., D: 4 min., E: 6 min., F: 7 min., G: 10 min. after antigen administration. Spike potentials retouched.

fails to return to the control values. The frequency of impulses increases, but reach lower values than in group 3 a. The shortening of the inactive phase (SP) is correlated in time with the changes of the remaining parameters; it passes the control values associated with the persistent shortening of the duration of volleys. Fig. 9 illustrates the changes described.

DISCUSSION

According to our assumptions the excitation of vagal motoneurons in anaphylactic shock (17) is accompanied by the corresponding reaction of the phrenic motoneurons. The respiratory centres of the medulla are probably "pacemakers"

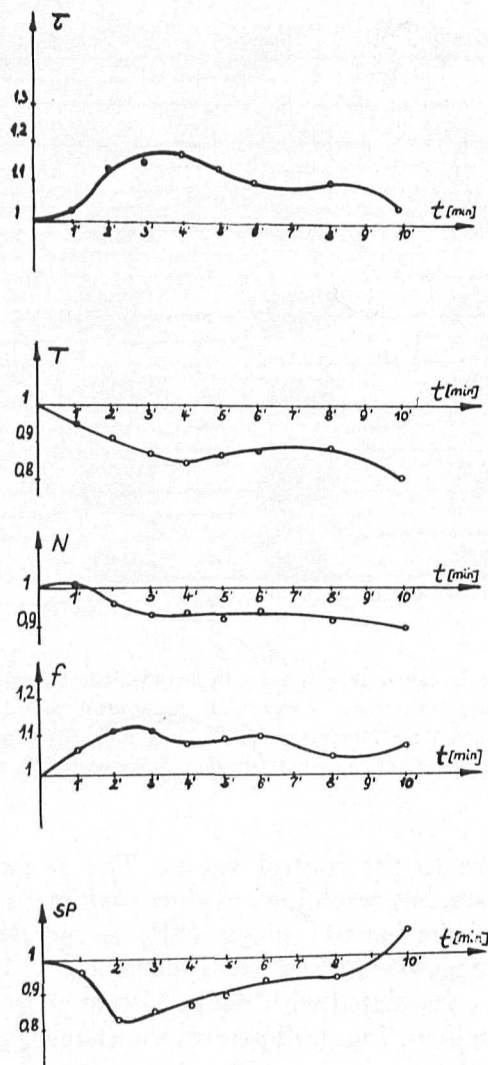


Fig. 8.

Diagram of reaction of phrenic motoneurons of vagotomized, artificially ventilated animals. τ : frequency of volleys.

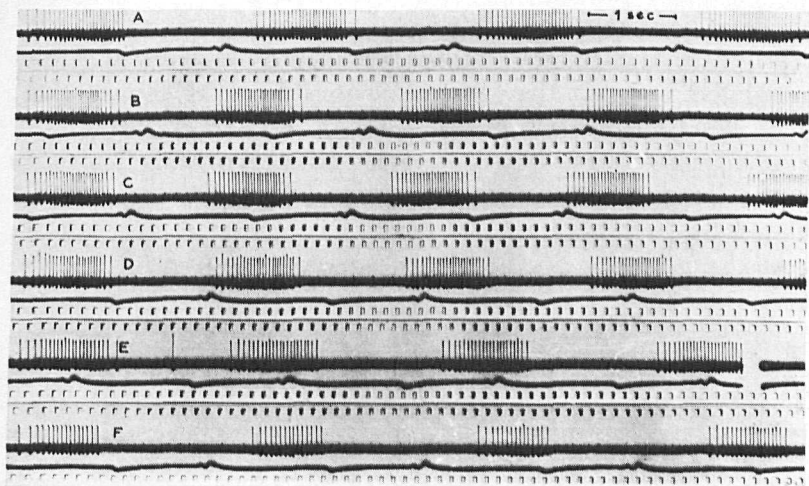


Fig. 9.

Changes in phrenic motoneuron activity in anaphylactic shock. Animal artificially ventilated, bilaterally vagotomized. Lower tracing: respiratory pump rhythm. A: control record 12 min. after bilateral vagotomy, B: 2 min., C: 4 min., D: 6 min., E: 8 min., F: 10 min. after antigen administration.

for both vagal and phrenic motoneurons (6). Nevertheless there is no close correlation between the contraction of inspiratory muscles and the activity of vagal motoneurons (18). The enhancement of phrenic motoneuron activity in anaphylactic shock described in this paper illustrates an increased work of the diaphragm. This work would attempt to overcome the resistances of constricted airways and probably the disturbances in pulmonary circulation. Enhanced activity of phrenic motoneurons has been described in response to respiratory loads (13), and as a response to the increased air-flow resistance in anaphylactic shock in guinea-pigs (9). An appearance of tonic activity in phrenic motoneurons in part of the experiments corresponds to the tonic contraction of the diaphragm and would tend to maintain the diaphragm in an inspiratory position. This fact is the quantitative parallel of the increase of phrenic motoneuron activity described

above. The change in activity of the phrenic nerve might correspond to the collapse of the respiratory alveoli in hypoventilated parts of the lungs. Previously it was shown, that lung deflation causes an increase of discharges in phrenic motoneurons (12). The afferent pathway of this reflex is probably going through the vagal fibres from receptors stimulated by lung collapse (7, 10). Experimental data show, that the majority of the phrenic nerve fibres constitute the efferent pathway transmitting information from respiratory "centres" via spinal motoneurons to the diaphragm. The afferent fibres constitute only 10 per cent of the phrenic nerve (19). This fact suggests that with such a little percentage of afferent fibres the afferent pathways from the lungs may have an important role as a sensory input to the "centres" (1). The measure of dependence of the activity of phrenic motoneurons on vagal afferentation is indicated by its less significant enhancement after bilateral vagotomy. The persistence of some changes in phrenic nerve activity in anaphylactic shock after vagotomy seems to indicate the importance of information also from extravagal sources. The excitation of phrenic motoneurons might be determined by the same factors which influence the respiratory "centres" and vagal motoneurons in anaphylactic shock as discussed in detail in a preceding paper (17).

It is necessary to underline the role of the intercostal-to-phrenic reflex recently described (3) which could be an important link in excitation of the phrenic nerve nuclei and in the regulation of respiration, and could explain the changes in phrenic nerve activity in artificially ventilated, bilaterally vagotomized animals.

The activity of phrenic motoneurons is the exponent of the activity level in the respiratory "centres". Therefore all primary and secondary factors which influence the course of anaphylactic shock must be taken into account in considering the sources of information which adapt the organism to the altered conditions associated with anaphylactic shock.

SUMMARY

The bioelectric activity of phrenic motoneurons in anaesthetized rabbits was recorded in anaphylactic shock. An enhanced activity (appearance of tonic frequency-modulated activity and increase in the mean frequency of impulses) was found. The alteration could illustrate increased diaphragmatic work attempting to overcome the increase of total lung resistance. The enhancement of phrenic motoneuronic activity was reduced but not abolished by vagotomy. This suggests the presence of extravagal sources which supply information to the respiratory "centres".

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