STUDIES ON THE CENTRAL EFFECTS
OF HERING–BREUER REFLEXES

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Abstract. In our previous experiments performed with rabbits, it was found out that the strength of both inflation and deflation Hering-Breuer reflexes depends on the level of anaesthesia and ventilation as correlative factors in spontaneously and artificially ventilated animals, though this dependence was quantitatively and qualitatively different in these two groups. On the basis of the recent evidence pointing to the rapidly conducting fibres and thus indirectly the pulmonary stretch receptors as the pathway along which both Hering–Breuer reflexes are transmitted, an attempt has been made to show how both parameters of ventilation are centrally controlled in response to afferent information concerning such mechanical factors as resistance and compliance of the respiratory system. The results presented seem to allow the following conclusions: (i) An important role may be ascribed to the pulmonary stretch receptors in transmission of both Hering–Breuer reflexes. (ii) In quiet breathing the central mechanisms of the Hering–Breuer inflation reflex are set to regulate tidal volume on the basis of analysis of the compliance of the respiratory apparatus at the given moment. Their role to the control of the respiratory frequency is of minor importance. (iii) The contribution of the pulmonary stretch receptors to the control of respiratory frequency is based on information about the resistance of the airways. This parameter influences the ratio of duration of the activity phase to silent phase in discharges of pulmonary stretch receptors.

Recent investigations on the Hering–Breuer reflexes have supplied a number of data indicating the dependence of these responses on the level of anaesthesia (Bystrzycka and Huszczuk 1969, Bouverot et al. 1970, Bystrzycka et al. 1972, Bystrzycka et al. 1971). This applies first of all to the inflation reflex. We demonstrated that the deepening of anaesthesia may enhance the Hering–Breuer inflation reflex only as long as the

function of the respiratory and circulatory systems remain undisturbed by anaesthesia. Furthermore, as shown in Fig. 1, the strength of the Hering–Breuer inflation reflex is exponentially dependent on the level of ventilation. The activity of the phrenic nerve was assumed to reflect the level of ventilation. Thus, a diminished amplitude of phrenic nerve
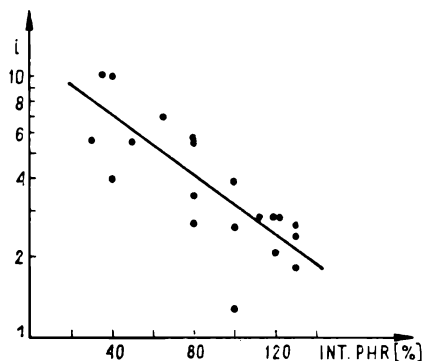

Fig. 1. Dependence of coefficient i on the level of integrated phrenic nerve activity in artificially ventilated rabbits. (From Bystrzycka et al. 1971.)

discharges corresponded to an increase in ventilation. The inhibition coefficient (i) was determined as the ratio of the duration of the silence period which followed the applied inflation to the duration of the control expiratory pause. It results from the plot that there is a linear relationship between the logarithm of the inhibition coefficient (i) and the phrenic nerve amplitude.

As regards the deflation reflex, we have demonstrated that its strength also depends on the level of anaesthesia as represented in Fig. 2. The values of the coefficient (e) were determined as the ratio of the
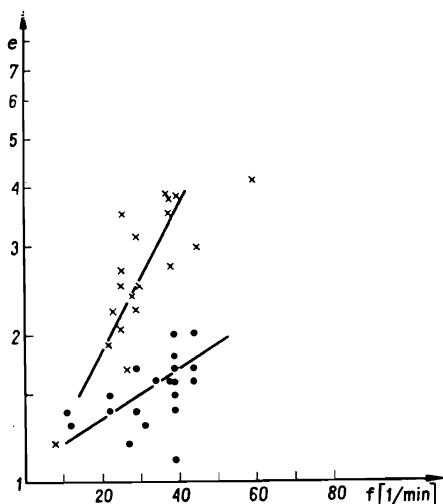

Fig. 2. Coefficients of excitation e plotted against rate of breathing for natural (dots) and forced (crosses) deflation in spontaneously breathing rabbits. (From Bystrzycka et al. 1971.)

duration of inspiration following deflation to the duration of the preceding control inspiration. Deflation was produced in two ways: either by preventing inspiration (marked by dots), or by applying negative pressures at the order of 5 cm of water (marked by crosses); the latter manoeuvre produced tracheal pressure changes approximately twice those of the former. The value of the control respiratory frequency was assumed as criterion for estimation of the depth of anaesthesia. The plot shows that the strength of the deflation reflex depends both on the value of the control respiratory rhythm and on the negative pressure applied.

Since the depth of anaesthesia influences the values of coefficients i and e in an opposite manner one could, therefore, consider the Hering–Breuer inflation and deflation reflexes as the complementary mechanisms. These might be produced either by inhibition or excitation of the central inspiratory activity, depending on the frequency of vagal afferent information transmitted via rapidly conducting fibres. This concept agrees with the experimental data obtained by Wyss (1954ab) who demonstrated that stimulation of the rapidly conducting fibres at low frequencies enhances the inspiratory action whereas the high frequency stimulation inhibits the central inspiratory activity. In the light of Paintal's (1966) evidence for "frequency dependence" of vagal cold block, Head's paradoxical reflex (1889) might be considered as further confirmation of this hypothesis.

On the basis of the foregoing and the recent experimental evidence indicating the participation of the pulmonary stretch receptors in transmitting both Hering–Breuer reflexes (Guz et al. 1970, Luck 1970, Guz and Trenchard 1971, Koller et al. 1971) we decided to verify this hypothesis by means of a quite different experimental model.

We assumed that the frequency of the stretch receptor discharges defines the lung volume as follows:

$$f = k \cdot V^n$$

where the value of the coefficients k and n is not important in this consideration.

The compliance is, in turn defined by the relation:

$$C_L = \frac{V}{P}$$

where P is a value of transpulmonary pressure.

Thus the volume can be given:

$$V = C_L \cdot P$$

and by substituting into the first equation we get:

$$f = k (C_L \cdot P)^n$$

It results from this formula that the discharge frequency of the pulmonary stretch receptors depends on the compliance of the respiratory apparatus. Since transpulmonary pressure (P) exists virtually only during the inspiratory phase, the pulmonary stretch receptors in this phase transmit information defining the value of the compliance.

The resistance of the airways may be described by the relation:

$$R = \frac{p}{V} \cdot t$$

where p is a pressure drop along the respiratory tract.

After a similar transformation we get that:

$$V = \frac{p}{R} \cdot t$$

and finally by substituting into the first equation we get:

$$f = k \left(\frac{p}{R} \cdot t \right)^n$$

Thus, discharge frequency of a pulmonary stretch receptor also supplies information about resistance of the airways, the relation being inversely proportional. The existance of this relation is important during the expiratory phase, since the parameter p does not disappear in this phase, only its sign changes.

Therefore two types of discharges from pulmonary stretch receptors should be distinguished. Firstly phasic discharges signalling during inspiration the value of compliance of the respiratory apparatus at the given moment. Their role would be limited to the regulation of the depth of breathing. Secondly, tonic modulated activity would supply information as to the resistance of the airways and would be responsible for the regulation of the respiratory rhythm.

In order to check whether these conclusions are true, two experimental techniques were used.

The first served for a possible accurate simulation of compliance changes in the respiratory apparatus. This could be achieved by changing the gain of the respirator controlled by the integrated activity of the phrenic nerve (Huszczuk 1970). The response of the respiratory centres to this manoeuvre was investigated in paralysed and non-paralysed rabbits with intact vagi and anaesthetized with pentobarbitone (25 mg/kg). Figure 3 shows examples of records from this group of experiments. At the points marked by arrows the gain was reduced or increased; this resulted in practice in an increase or decrease of the air-volume forced into the lungs at a given level of phrenic activity. In general, immediate
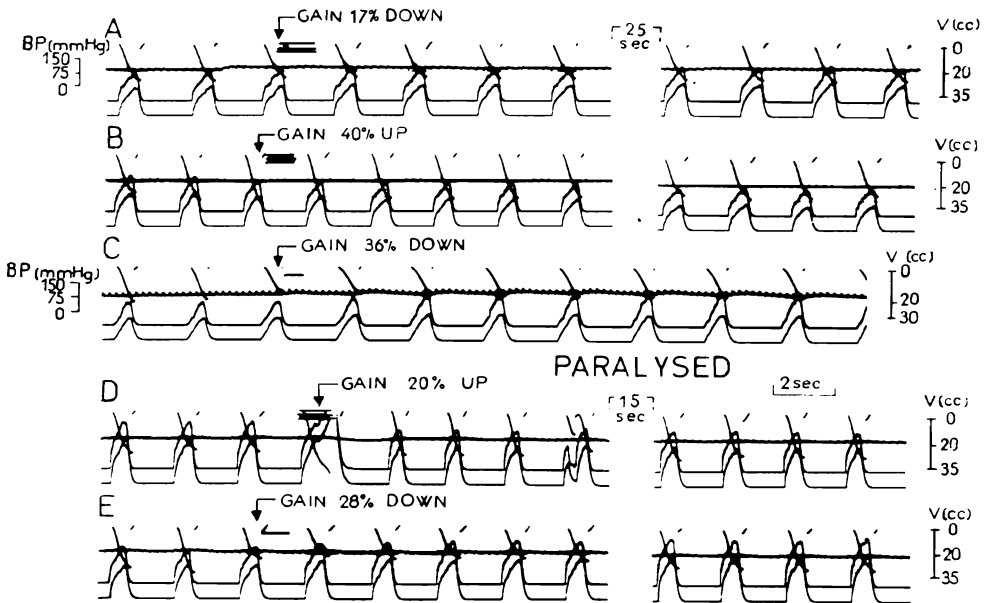
NON PARALYSED

Fig. 3. Responses of the integrated phrenic nerve activities to step changes of servo-system gain of the phrenic nerve controlled respirator in non-paralysed (records A, B and C) and paralysed (records D and E) rabbits. For each record from above down: inspired tidal volume (deflection downwards); arterial blood pressure and integrated activity of the left and right C_3 roots of the phrenic nerves.

changes in the activity of the phrenic nerve reflected an attempt to compensate for the consequence of the manoeuvre applied. It is worth noting that the compensation involved only the volume (statistically significant), but not the respiratory frequency (statistically not signifi-

TABLE I

Responses to rise and fall of compliance simulated by step changes of servo system gain by $\pm 25\%$ of the phrenic nerve controlled respirator (mean results from 12 experiments)

Experimental conditions		Mean responses (in per cent)$\pm$SE			
		Respiratory rhythm	Tidal volume	Integrated phrenic nerve activity (C_3 root)	
				left	right
Non-paralysed	gain up	$+2.9\pm1.9$	$+5.9\pm2.5$	-10.8 ± 2.4	-11.5 ± 2.3
	gain down	$+1.8\pm1.6$	-4.3 ± 1.3	$+25.4\pm3.8$	$+19.6\pm4.6$
Paralysed	gain up	$+8.3\pm4.8$	$+12.0\pm7.6$	-17.5 ± 2.15	-17.0 ± 2.0
	gain down	0 ± 2.5	-15.8 ± 2.4	$+27.0\pm8.3$	$+25.6\pm8.1$

cant). Table I shows the mean results. The compensating response to changes simulating decrease in compliance seems to be more effective both in the group of paralysed and non-paralysed animals. The quantitative differences between these groups seem to be due to the elimination of the intercostal muscles from the process of compensation in paralysed animals.

The other experimental technique consisted in a stimulation of the central end of the vagus nerve with pulses from a generator triggered by the simultaneously recorded activity of a pulmonary stretch receptor (Fig. 4). The stimulation reduced the duration of the respiratory cycle

Fig. 4. Experimental set-up used in the experiments with the triggered stimulation.

and the amplitude of inspiration, thus producing a picture similar to that before vagotomy (Fig. 5ABC). After switching off the stimulation respiration returned to the pattern characteristic for post-vagotomy states in animals breathing spontaneously (Fig. 5D). The strength of stimulation was adjusted so as to obtain a respiratory frequency close to that noted before vagotomy. Too strong stimulation produced first apnoea and then breathing of a rapid and shallow type (Fig. 6).

Under the conditions of triggered stimulation we could observe responses to inflation and deflation of the lungs. Figure 7 presents the
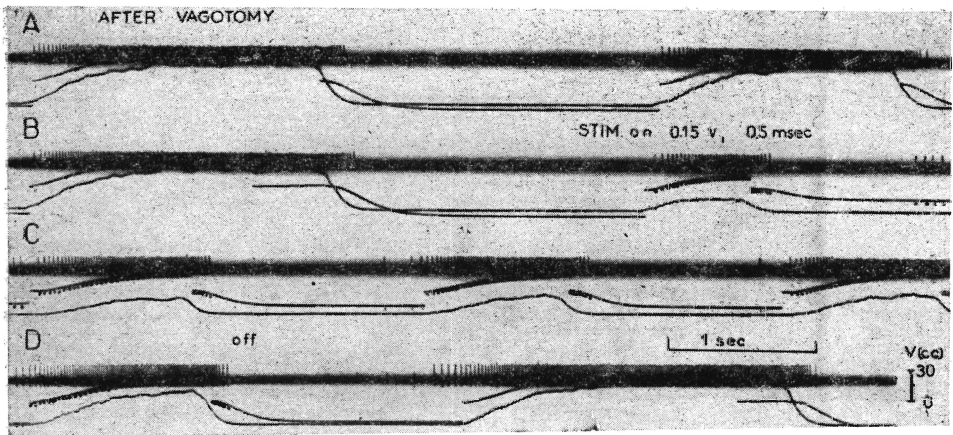
Fig. 5. Typical response of the activity of pulmonary stretch receptor (top trace), tidal volume (middle trace) and integrated phrenic nerve activity (bottom trace) to triggered stimulation. A, control record; B, triggered stimulation on; C, steady state; D, triggered stimulation off. Pulses are superimposed on the pneumotachograph record when stimulation on. (In this Figure and Fig. 7, 8 and 12 these pulses are retouched.)
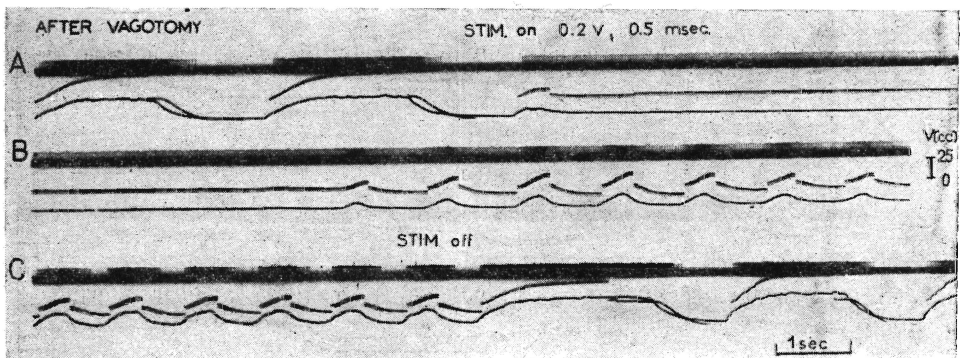

Fig. 6. Pattern of breathing obtained with strong stimulation. A, stimulation on; B, continuation of A; C, steady state and stimulation off. Traces as in Fig. 5

response to a smaller and larger lung inflation. At larger inflation (Fig. 7CD) the component of Head's paradoxical reflex was frequently observed preceding the period of inhibition of inspiratory activity. Deflation of the lungs caused a characteristic response in the form of a distinct excitation of the phrenic nerve activity (Fig. 8). The pulmonary stretch receptor activity showed a considerably reduced frequency of impulses during deflation. Figure 9 shows the response to lung inflation and deflation. The fact of simultaneous recording of two pulmonary stretch receptors activities one of which responds to inflation and the other, with lower ampli-
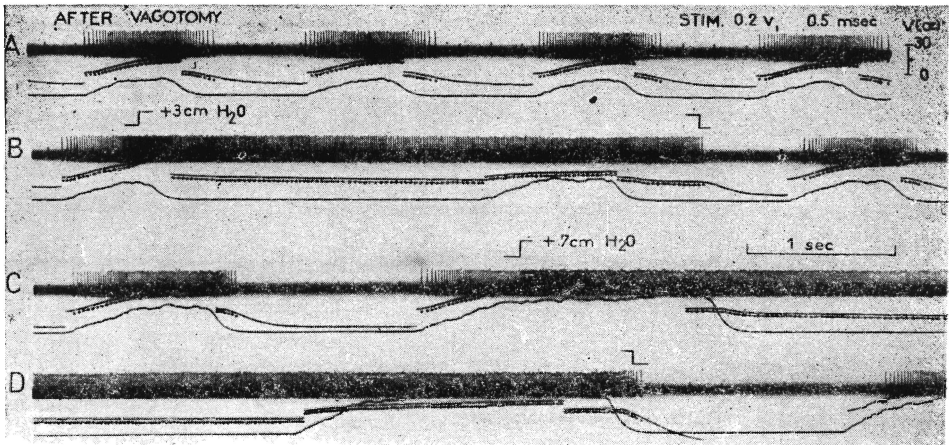
Fig. 7. Responses to a small, and to a large, lung inflation. *A*, control record; *B*, small inflation; *C*, large inflation; *D*, continuation of *C*. Traces as in Fig. 5.
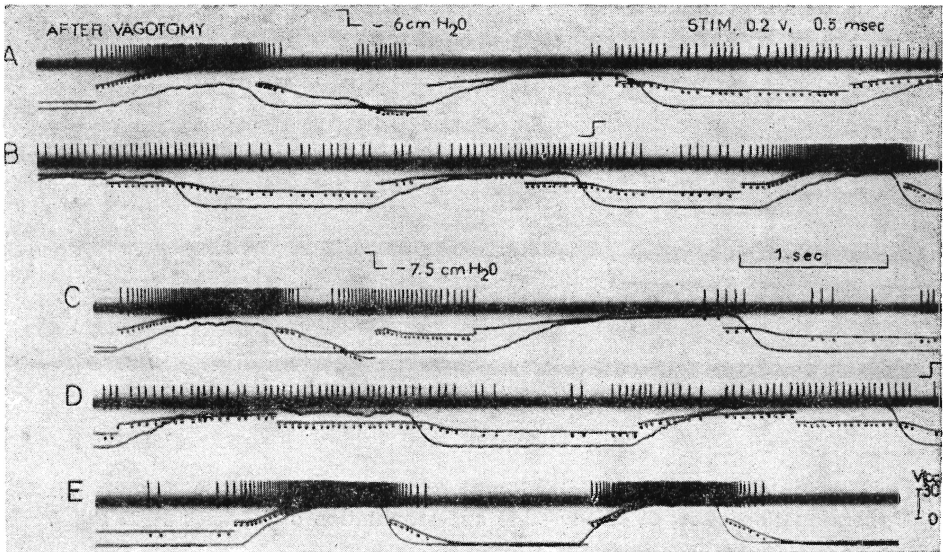

Fig. 8. Example of responses to lung deflation. *A*, deflation — 6 cm H_2O; *B*, continuation of *A*; *C*, deflation — 7.5 cm H_2O; *D*, continuation of *C*; *E*, continuation of *D*. Traces as in Fig. 5.

tude to deflation, should be noted here. The generator was triggered by the discharge of a higher amplitude.

Under similar experimental conditions the response to histamine injection, cigarette smoke and ammonia vapour have been checked (Fig. 10–12). These stimuli caused in many cases rapid and shallow breathing.
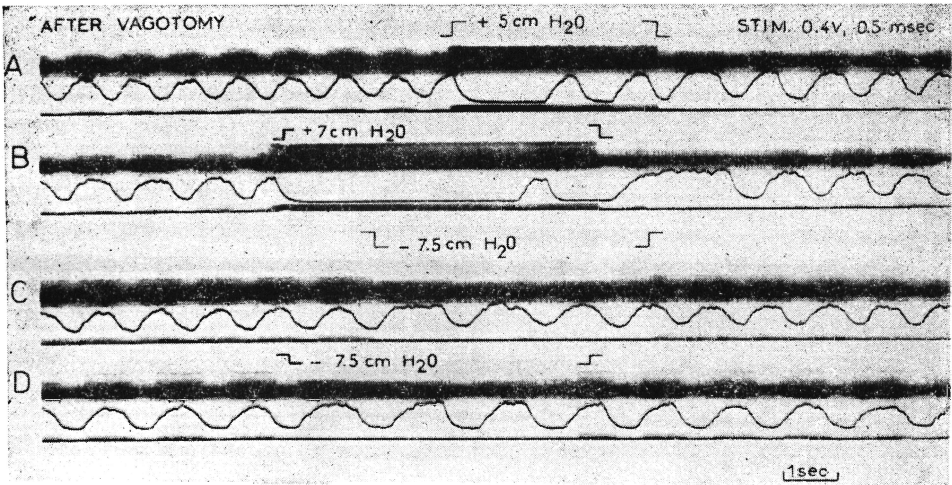
Fig. 9. Responses to lung inflations (A and B) and deflations (C and D). Record of two pulmonary stretch receptor activities (top trace), integrated phrenic nerve activity (middle trace) and triggered stimulation marker (bottom trace).
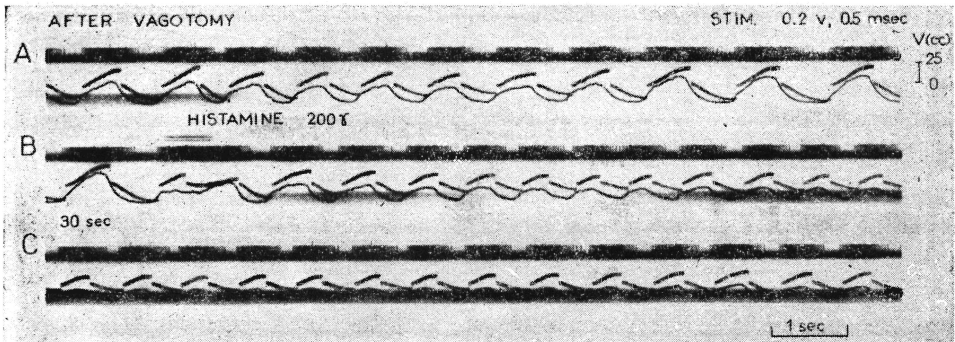

Fig. 10. Response to histamine injection during triggered stimulation. A, control record; B, injection of histamine; C, 30 sec latter. Traces as in Fig. 5.

This was sometimes accompanied by a modulated activity of the pulmonary stretch receptor. In response to ammonia vapour, continuous, frequency-modulated activity characteristic for bronchoconstriction was observed (Fig. 12CDE). After switching off the stimulation modulated activity gradually returned to phasic activity.

The results presented seem to allow the following conclusions:

1. An important role may be ascribed to the pulmonary stretch receptors in transmission of both Hering–Breuer reflexes.

2. In quiet breathing the central mechanisms of the Hering–Breuer inflation reflex are set for a regulation of the tidal volume on the basis
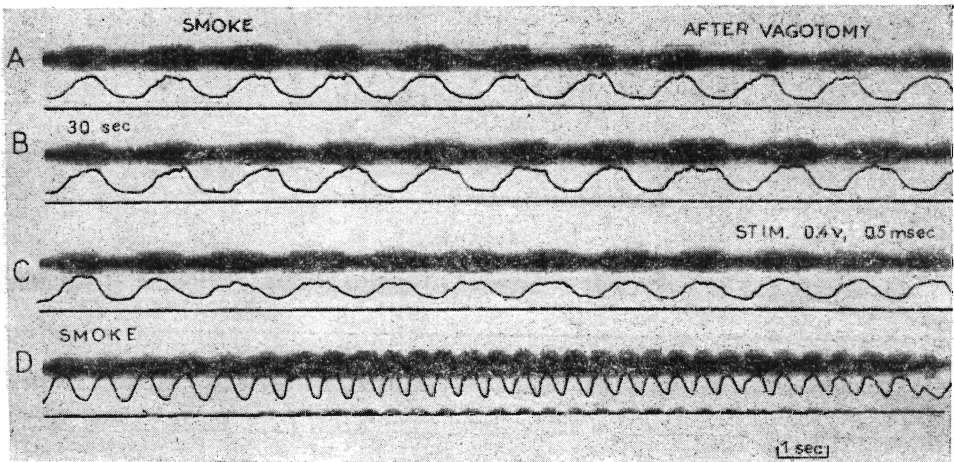
Fig. 11. Responses to cigarette smoke before (A and B) and during (D) triggered stimulation. C, control record for D. Traces as in Fig. 9.
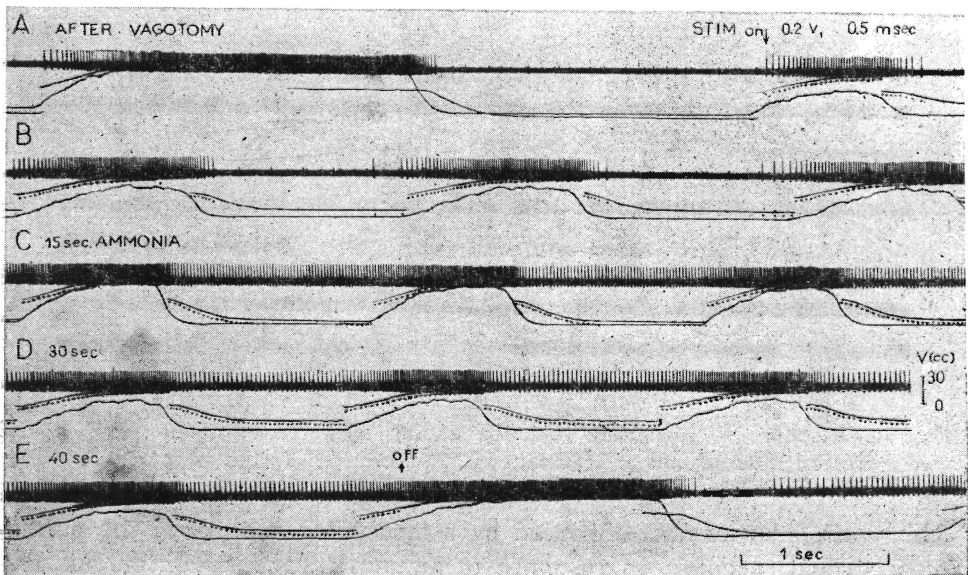

Fig. 12. Response to ammonia vapour. A, triggered stimulation on; B, continuation of A; C, 15 sec after ammonia vapour inhaled during two breaths; D, 30 sec after; E, triggered stimulation off. Traces as in Fig. 5.

of analysis of the compliance of the respiratory apparatus at the given moment. Their role in the control of the respiratory frequency is of minor importance.

3. The contribution of the pulmonary stretch receptors to the control

of respiratory frequency is based on information about the resistance of the airways. This parameter influences the ratio of duration of the activity phase to silent phase in discharges of pulmonary stretch receptors.

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