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CONTRIBUTION OF VARIOUS INSPIRATORY MUSCLES TO VENTILATION AND THE IMMEDIATE AND DISTANT EFFECT OF DIAPHRAGMATIC PARALYSIS

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Abstract. The contribution of the diaphragm and that of the other inspiratory muscles (scaleni and all the other extradiaphragmatic muscles) at different levels of tidal volume (V_T) and during static inspiratory efforts of various strengths has been studied in supine anaesthetized rabbits by blocking phrenic conduction with an electrotonic current. Rabbits spinalized at T_1 were used to measure the separate contribution of the scaleni. When the vagi are left intact there is an hyperactivity of the extradiaphragmatic muscles during the phrenic block which has been ascribed to Hering–Breuer reflexes. The relative contribution of the diaphragm to tidal volume, during quiet breathing, appears to approach 90% and is reduced to 75% during the maximum tidal volume attained. The scaleni appear to account for about 1/3 of the tidal volume contributed by all the other inspiratory extradiaphragmatic muscles during quiet breathing and their share goes up to 1/2 at the highest ventilation. The contribution of the scaleni starts at the same level of inspiratory output found for all extradiaphragmatic muscles and therefore these muscles should not be considered "accessory" Within the range of V_T considered the sternomastoids did not appear to contribute, as shown by the fact that their disinsertion did not change the results obtained in spinalized rabbits. Immediately after block of the phrenic nerves there is a marked decrease of V_T which then increases within 10–15 breaths to a steady value, three to four times that of the first breath after the paralysis, which is maintained thereafter. The respiratory frequency decreases immediately to a slightly lower value after phrenic block in control animals and does not change when the vagi are cut. In any case a fairly steady value is maintained thereafter even when various types of stimulation are applied. Only changes in body temperature could change respiratory frequency. Chronically phrenicectomized rabbits show some compensatory phenomena either functionally or morphologically. They become able to change their ventilation when chemical drive is increased. In the external intercostal muscles the myoglobin concentration increases and ultrastructural modifications become apparent.

The inspiratory contribution of the diaphragm and the other muscles having an inspiratory activity has been measured directly in the anaesthetized supine rabbit by blocking conduction in the two phrenic nerves and therefore paralysing the diaphragm at different levels of inspiratory activity (Fig. 1).

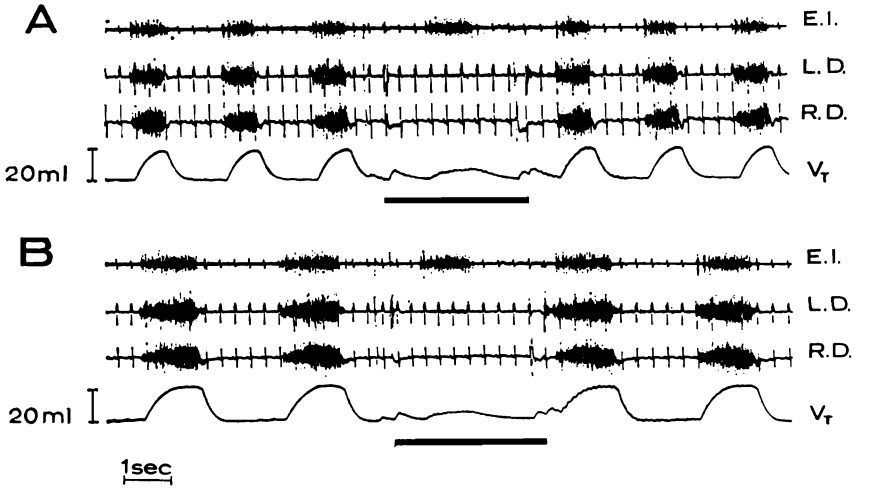

Fig. 1. Anaesthetized rabbit. Bilateral block of both the phrenic nerves (anodal). *A* before, *B* after vagotomy. The heavy lines indicate duration of phrenic block. E. I., EMG from external intercostal muscle; L. D., EMG from left hemidiaphragm; R. D., EMG from right hemidiaphragm; V_T, tidal volume. When the d–c current is applied to the phrenic nerves for the blocking a contraction of the corresponding hemidiaphragm is observed on closing and on opening the circuit; this is visible both in the EMG and in the V_T tracings. The ECG is also present in the EMG tracings. (From Sant'Ambrogio et al. 1966.)

The nervous output to an extradiaphragmatic inspiratory muscle, as measured by the action potentials from single fibres, increases even in the first breath during diaphragmatic paralysis when the vagi are intact, but does not change if the vagi are cut (Sant'Ambrogio et al. 1966) (Fig. 2). The hyperactivity of the extradiaphragmatic muscles during phrenic blockade with intact vagi has been ascribed to Hering–Breuer reflexes (Dolivo 1952, Sant'Ambrogio et al. 1966). In vagotomized rabbits these compensatory mechanisms are absent and the results should therefore be more indicative of the "true" contribution of inspiratory muscles in our experimental conditions.

The mechanical output of these muscles should be different when they are contracting simultaneously with the diaphragm, as in normal breathing, and during diaphragmatic paralysis; in fact during this latter

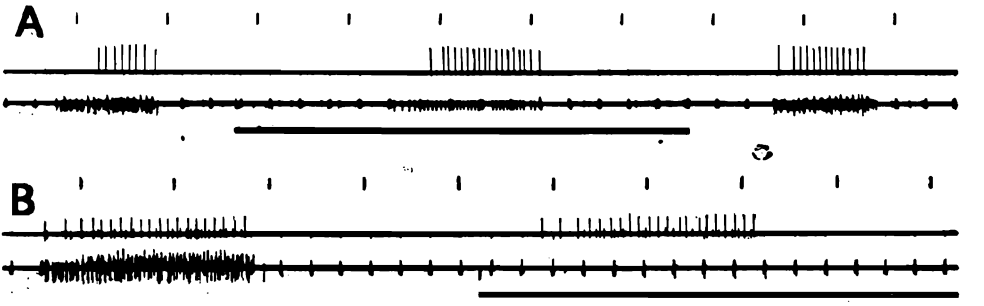

Fig. 2. Anaesthetized rabbit. Block of both phrenic nerves. *A* before, *B* after vagotomy. Top tracings, EMG from single fibre of external intercostal; bottom tracings, multifibre EMG from the whole diaphragm. The heavy lines indicate duration of phrenic block. During the blocking of the two phrenic nerves before vagotomy, *A*, the motor unit discharges for a longer time at a faster rate. No change in activity of the motor unit is seen after vagotomy (*B*). Time marker = 1 sec. (From Sant'Ambrogio et al. 1966.)

condition the extradiaphragmatic muscles are working at a much shorter length than in control breathing as indicated by the greater rib cage expansion (Fig. 3). From the force-length relationship of skeletal muscles it may be inferred that his condition implies a mechanical disadvantage of the extradiaphragmatic muscles. Therefore our method should increasingly underestimate their contribution as tidal volume (V_T) increases. On the other hand during static efforts (with closed airways) no consistent differences in the pressures developed by the extradiaphragmatic muscles are present between the values obtained with paralytic block or

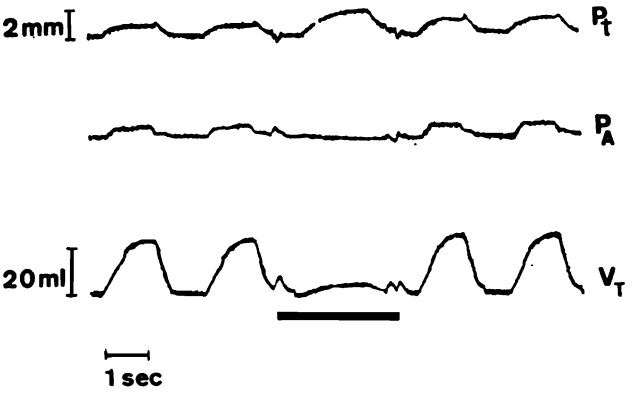

Fig. 3. Anaesthetized, vagotomized rabbit. P_t, thoracic circumference at the level of the xiphoid process; P_A, abdominal circumference below the rib cage; V_T, tidal volume. The heavy line indicates the duration of the anodal block of both the phrenic nerves. (From Provini et al. 1966.)

tetanic stimulation of the diaphragm (Mognoni et al. 1969). Nevertheless the length at which the extradiaphragmatic muscles are contracting in the two situations is quite different because in one case (paralysis) the rib cage is seen to expand while in the other it is seen to collapse (Mognoni et al. 1969). Therefore, at least during static efforts, the force-length relationship does not seem to be the only factor involved.

The same technique has been used on rabbits previously spinalized at T_1 in which the only extradiaphragmatic muscles are the neck muscles which derive their motor supply from the cervical spinal cord: C_4, C_5, C_6, C_7 and C_8 for the scaleni and C_2 and the spinal accessory for the sternomastoids. In these spinalized rabbits block of the diaphragm limits the inspiratory activity to the neck muscles, whose contribution can than be measured separately. The inspiratory contribution measured in these conditions should actually be ascribed only to the scaleni since the disinsertion of the sternomastoids did not alter the results (Sant'Ambrogio and Camporesi 1971).

The experimental data derived by paralyzing the diaphragm in non-spinalized and spinalized rabbits allow separate calculation of the relative contribution, to various levels of ventilation, of the scaleni, of the other extradiaphragmatic muscles and of the diaphragm (Fig. 4). The relative contribution of the diaphragm to tidal volume, during quiet breathing, appears to approach 90% and is reduced to 75% during the maximum tidal volume attainable. The scaleni appear to contribute about 1/3 of the tidal volume of all the other extradiaphragmatic muscles during quiet breathing and their share goes up to 1/2 at higher ventilation. The contribution of the scaleni starts at the same level of inspiratory output as that found for all extradiaphragmatic muscles and therefore these muscles should not be considered "accessory". Action potentials can be recorded from single muscle fibres of the scaleni during quiet breathing and either the peak frequency or the duration of their inspiratory discharge increases when the inspiration is hindered, whether the vagi are intact or are cut. This seems to indicate the presence of a proprioceptive mechanism acting during the inspiratory activity of these muscles.

In cats the inspiratory contribution of the diaphragm is less pronounced than in the rabbit, as shown in Fig. 5 which presents the ventilatory response to CO_2 before and after bilateral phrenicotomy (Sant'Ambrogio et al. 1970). In rabbits after phrenicotomy the extradiaphragmatic muscles seem to be working at their maximum capability and neither the V_T nor the respiratory frequency vary.

Immediately after block of the phrenic nerves there is a marked decrease of tidal volume which then increases within 10–15 breaths to a steady value, three to four times that of the first breath after the dia-

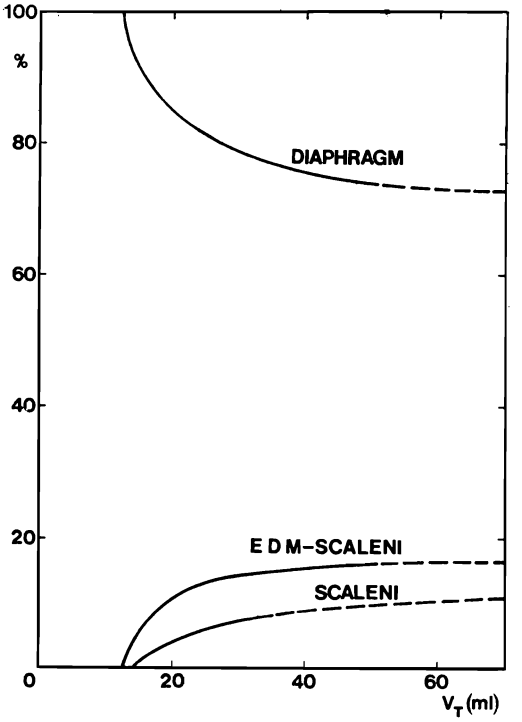

Fig. 4. The relative contribution of the scaleni (ordinate) for vagotomized rabbits, calculated from the data of Sant'Ambrogio and Camporesi (1971) together with that of extradiaphragmatic muscles other than the scaleni (EDM-scaleni) and of the diaphragm. (From the data of Mognoni et al. 1969, and Sant'Ambrogio and Camporesi 1971). The continuous lines cover the range of the experimental data, the interrupted lines extrapolate the results up to the value for inspiratory capacity (70 ml). (From Sant'Ambrogio and Camporesi 1971.)

phragmatic paralysis, which is maintained thereafter (Fig. 6). Respiratory frequency decreases immediately to a slightly lower value after phrenic block in intact animals (Fig. 6), due to an increase of inspiratory duration, whereas it does not change if the vagi have been cut. In any case a fairly steady value of respiratory frequency is maintained thereafter in spite of the increasing chemical drive to ventilation. Also painful stimuli do not change respiratory frequency; only changes in body temperature induce variation of respiratory rate.

The decrease in frequency of respiration noticed at the onset of diaphragmatic paralysis when the vagi are intact might be ascribed to a lesser stimulation of inflation receptors, and is also present when the airways are occluded. In both conditions there is a sort of functional denervation of the inflation fibres which allows a longer duration of the inspiratory discharge.

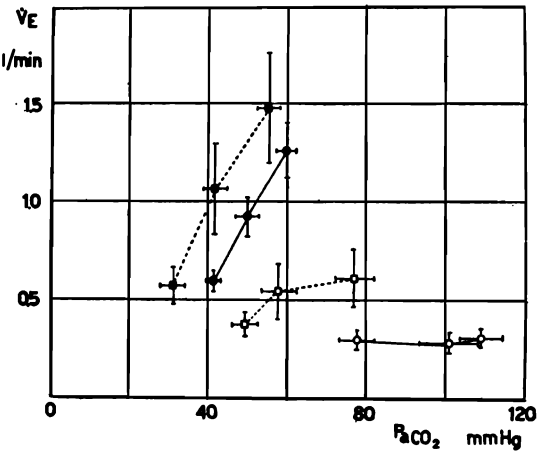

Fig. 5. $PaCO_2$-$\dot{V}_E$ relationships, average values, in anaesthetized rabbits (circles, continuous lines) and cats (squares, broken lines) before (filled symbols) and after (empty symbols) acute bilateral phrenicotomy. The standard errors are represented for each point. (From Sant'Ambrogio et al. 1970.)

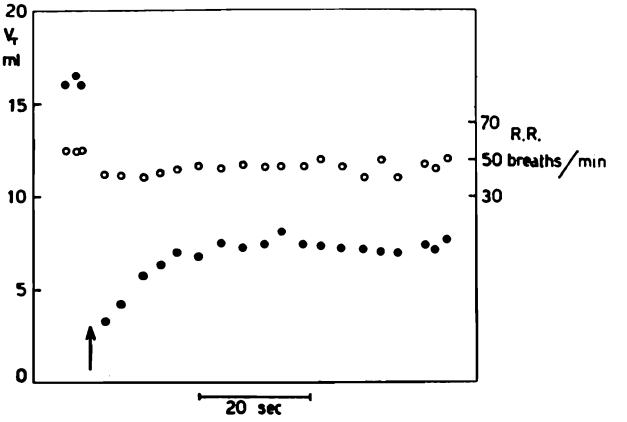

Fig. 6. Anaesthetized rabbit. Tidal volume (filled circles) and respiratory frequency (empty circles) taken breath before and after the induction of sudden paralysis of the diaphragm (arrow).

If for a rabbit rebreathing from a closed circuit V_T-$\dot{V}_E$ plots are drawn for intact nerves, for vagal block and for phrenicotomy with or without vagotomy, it may be noticed that after phrenicotomy the lower part of the plot coincides with that for vagal blockade, and that vagotomy does not add any further variation of the points obtained after section of the phrenic nerves (Fig. 7). On the other hand phrenic afferents do not seem to play a role in the regulation of respiratory activity, as shown

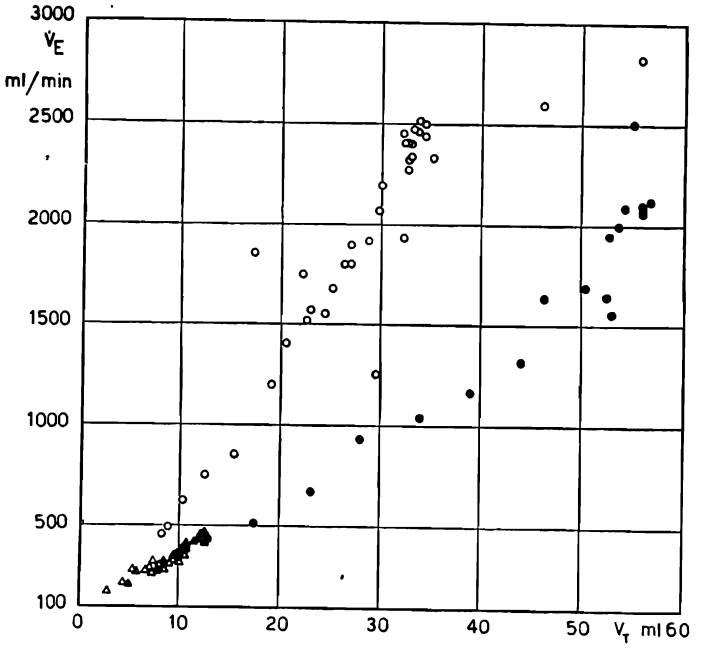

Fig. 7. V_T-$\dot{V}_E$ relationships for an anaesthetized rabbit rebreathing in a closed circuit after induction of hyperventilation apnoea through artificial ventilation before (○) and during (●) bilateral cold block of the vagi (no inflation and deflation reflexes), after phrenicotomy (△) and phrenicotomy plus vagotomy (▲).

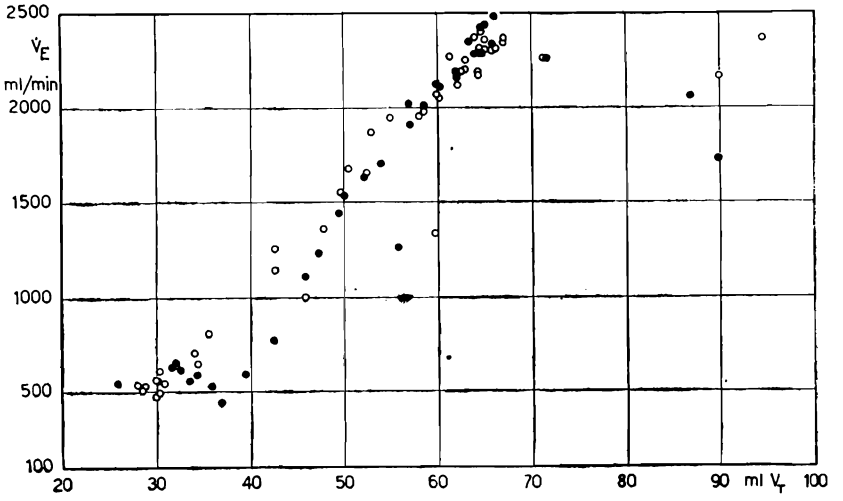

Fig. 8. V_T-$\dot{V}_E$ relationships for an anaesthetized rabbit rebreathing in a closed circuit before (empty circles) and after (closed circles) cervical dorsal rhizotomy.

by V_T-$\dot{V}_E$ plots obtained in a rabbit rebreathing from a closed circuit before and after cervical dorsal rhizotomy (Fig. 8). Also stimulation of the central cut-end of one phrenic nerve does not appear to vary the ventilatory response to chemical stimuli.

Chronically phrenicectomized rabbits show some compensatory phe-

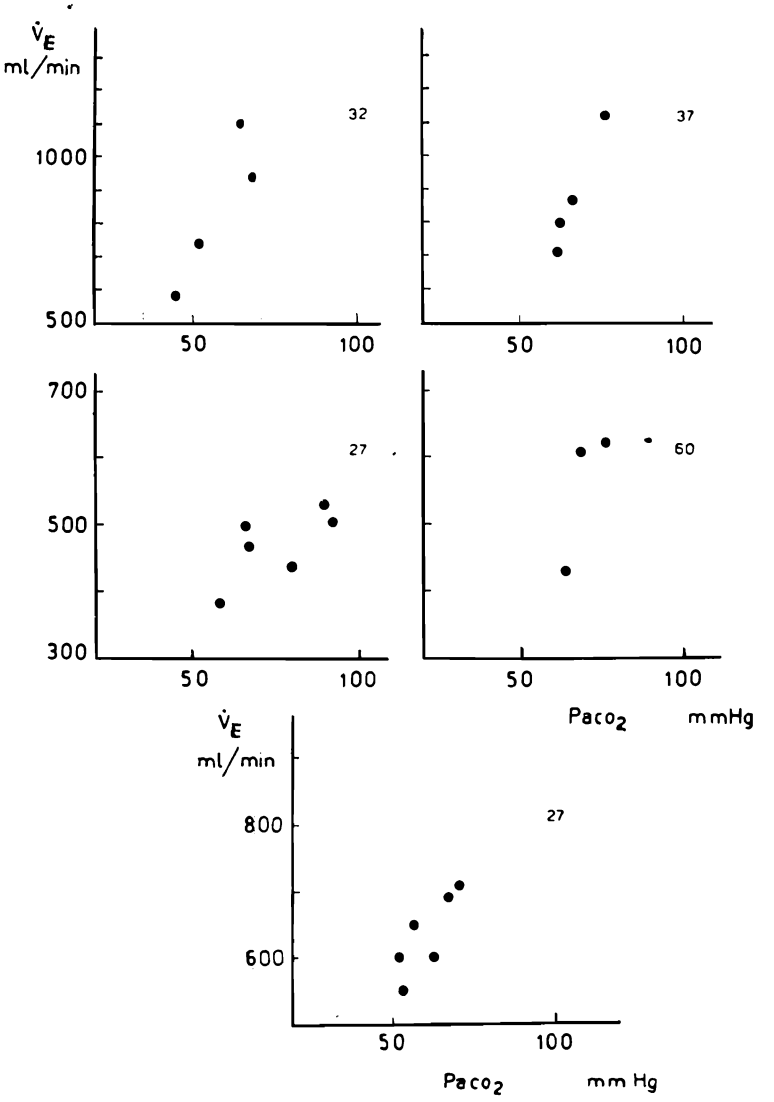

Fig. 9. $PaCO_2$-$\dot{V}_E$ relationships obtained in five rabbits which underwent bilateral phrenicectomy. The number at the right top corner of each individual graph indicates the days after the bilateral section of the phrenic nerves. (Sant'Ambrogio et al. 1970.)

nomena either functionally or morphologically (Sant'Ambrogio et al. 1970). They become able to change their frequency or tidal volume when the chemical drive is varied (Fig. 9). Ultrastructural modifications become apparent in rabbits phrenicectomized 1 month previously: the mean number of mitochondria in the external intercostal muscles is 2.5 times greater than in the controls and the mitochondria to fibre volume fraction is 3.8 times greater than in the controls. Myoglobin concentration is increased significantly only after 3 months from the phrenicectomy.

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