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MECHANISMS OF REGULATION OF RESPIRATION UNDER A RESISTIVE LOAD

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An increase in the nonelastic resistance to respiration (resistive loading) is known to cause a greater or lesser increase in the activity of the inspiratory muscles in man and animals, which may partly or completely compensate the additional load on the ventilatory apparatus [1, 6-9]. However, the mechanism of this response has not been adequately studied, in particular, the role which the afferent system of the lungs plays in its formation.

In this investigation a physiological analysis was undertaken of responses of respiration of intact and vagotomized cats to resistive loading, acting against the background of quiet breathing or of hyperpnea caused by progressive hypercapnia.

EXPERIMENTAL METHOD

The following parameters were recorded in 33 tracheotomized cats under urethane-chloralose anesthesia, during quiet breathing and with an additional inspiratory resistance equal to 380 cm water/liter/sec: electrical activity of the phrenic nerve (APN), the peak inspiratory intrathoracic pressure (P_I), the respiratory volume (V_T), the duration of inspiration (T_I), the mean velocity of the inspiratory flow ($\dot{V}_I$), and the partial CO_2 pressure of the alveolar gas (P_{ACO_2}). The technique of recording these various parameters and the method of creating the resistive load were described previously [3-5]. In series I the animals breathed air and the additional resistance was introduced at the second minute. The responses to this load were recorded in the transitional (the first respiratory cycle after addition of the resistive load) and stable (end of the second minute of respiration against additional resistance) periods. In series II the animals breathed oxygen in a closed system, with a gradual increase in P_{ACO_2} from 35 to 57 mm Hg. Rebreathing lasted 3-4 min and took place under quiet breathing or resistive loading conditions. In both series each test was carried out before and after division of both vagus nerves in the neck. Statistically significant ($P \leq 0.05$) changes in the parameters tested due to the action of loading are given below.

EXPERIMENTAL RESULTS

In the experiments of series I (Fig. 1) introduction of the additional resistance caused a rapid rise in APN and P_I as well as a decrease in V_T and slowing of $\dot{V}_I$. Consequently, as early as during the first "loaded" inspiration, the mechanism increasing the inspiratory activity of the respiratory muscle had begun to act. The response observed was not due to intensification of chemoreceptor stimuli. Humoral changes caused by hypoventilation developed later: Toward the end of the second minute of respiration against the additional resistance P_{ACO_2} increased on average by 1 mm Hg. The further increase in APN and P_I, and also the restoration of V_T and $\dot{V}_I$ to their initial levels (during quiet breathing), observed by that time, must also be explained by intensification of chemoreceptor stimulation.

After vagotomy APN, P_I, V_T, and T_I were increased, but $\dot{V}_I$ showed no significant change under these conditions. Resistive loading no longer increased APN, whereas the increase in P_I was maintained. This sug-

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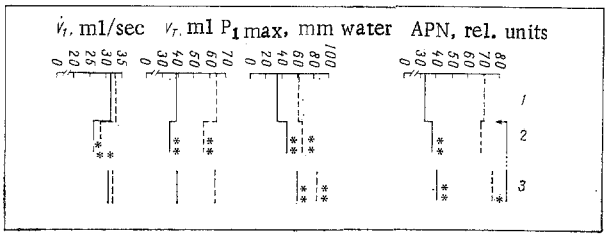

Fig. 1. Changes in parameters of respiration of cats under resistive loading. 1) free respiration; 2) first "loading" respiratory cycle; 3) respiration with resistive loading under steady-state conditions. Continuous line – before vagotomy, broken line – after vagotomy. *) differences compared with background (free respiration) significant at $P \leq 0.05$ level, **) at $P \leq 0.01$ level.

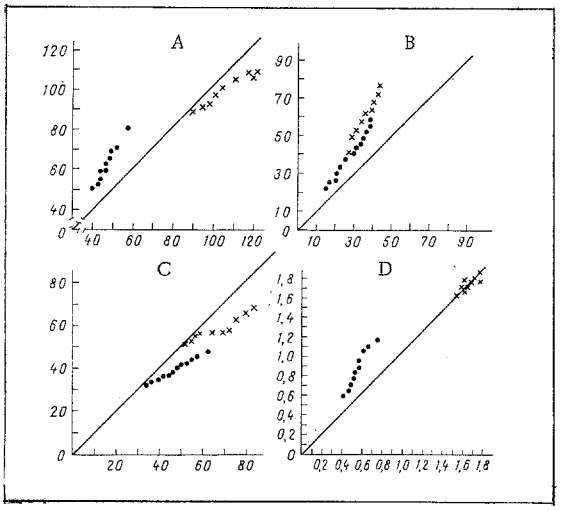

Fig. 2. Effect of resistive loading on parameters of free respiration in cat during progressive hypercapnia. A) APN, relative units, B) P_1, mm water; C) V_T, ml; D) T_1, sec. Circles – before vagotomy, crosses – after vagotomy. Each point shows values obtained at the same P_{ACO_2} level during free respiration (horizontal scale) and resistive loading (vertical scale).

gests that the response of the diaphragmatic motoneurons to the additional resistance to respiration was mediated through the afferent system of the lungs, but when the latter was blocked, yet another mechanism of compensation of the resistive load appeared. However, in the steady state the effect of this mechanism could be masked by the hypercapnic shift mentioned previously.

The experimental series II were therefore carried out. Using a rebreathing method to create progressive hypercapnia, the values of the various parameters were compared during free respiration and under resistive loading, with strictly equal values of P_{ACO_2} (Fig. 2). These experiments showed that the additional resistance reduced the increase in V_T and $\dot{V}_1$ and the shortening of T_1 due to hypercapnia, but increased APN and P_1. In the vagotomized animals resistive loading caused no longer an increase, but a moderate decrease in the response of APN to progressive hypercapnia. The effect of loading on T_1 also disappeared. Nevertheless, P_1 increased in response to the added resistance, and this led to an increase in V_T parallel to the rise in P_{ACO_2}, although by a lesser degree than during free respiration.

Consequently, under the influence of resistive loading mechanisms are activated, one of which leads to intensification of afferent activity of the phrenic centers in connection with the functions of the afferent sys-

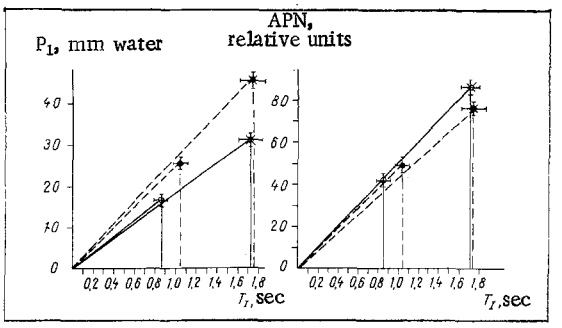

Fig. 3. Effect of resistive loading on rate of rise of APN and P_1 in cats during inspiration. Empty circles and continuous lines denote free respiration, filled circles and broken lines respiration against resistive load. Crossed out circles – the same after vagotomy. Short horizontal and vertical lines indicate standard errors of means.

tem of the lungs, whereas the others increase the respiratory effort in other ways.

Let us examine the first of these mechanisms. The Hering-Breuer reflex from the mechanoreceptors of the lungs, the pathway for which includes afferent fibers of the vagus nerve, inhibits the increasing activity of the inspiratory neurons of the respiratory center as inspiration develops, and interrupts inspiration; moreover, the greater the amount and rate of stretching of the lungs, the sooner inspiration is interrupted. In the present experiments resistance reduced both the volume (V_T) and the dynamics ($\dot{V}_1$) components of stretching of the lungs, which reduced activation of the corresponding receptors [2] and must have delayed the time of interruption of inspiration. In that way, the maximal achievable inspiratory activity was increased. In fact, as Fig. 3 shows, resistive loading did not affect the rate of growth of APN during inspiration (APN/T_1), and the maximal value of APN was increased only on account of lengthening of the inspiratory phase, although V_2, because of the additional resistance, was unable to reach a level which would correspond to increased activity of the phrenic motoneurons. It will be clear from the results given above that resistive loading does not directly affect the level of central inspiratory activity. The increase in the maximal values of this parameter took place only as a result of lengthening of the corresponding phase of the respiratory cycle. After vagotomy there is no lengthening of T_1 and this mechanism no longer operates.

However, by contrast with APN, the rate of rise of P_1, reflecting the total effort of the muscles responsible for inspiration, increased under the influence of resistive loading. This reflects the participation of compensatory mechanisms unconnected with the response of the phrenic motoneurons and the stretch receptors of the lungs. In fact, after vagotomy the quickening of the rise in P_1 caused by the additional resistance was even more marked and took place against the background of reduced activation of the diaphragm. This may perhaps be the result of activation of other muscles – intercostal and abdominal. The involvement of these muscles may be brought about through a "load compensating" reflex [10], including activation of muscle spindles and α-motoneurons as the result of disparity between the length of the extra- and intrafusal fibers during an increase in the resistance to inspiration. Meanwhile, an important role in the compensation of the additional mechanical load may be played by the "internal properties" of the muscles themselves, in this case the inspiratory muscles – their ability to develop a greater effort during an increase in operant length and slowing of contraction [11, 12].

The facts described above are evidence of the multiplicity of mechanisms participating in the biologically important response of the ventilatory apparatus to resistance to respiration.

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