COMBINED ACTION OF HYPOXIA, HYPERCAPNIA, AND ADDITIONAL RESISTANCE ON RESPIRATION IN MAN

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The dynamics of the ventilation and composition of the alveolar air and blood gases during respiration were investigated in ten healthy men with normal and increased (by up to 20 cm water/liter/sec) resistance. During the tests, the subjects breathed either air or a hypoxic, hypercapnic, or combined hypoxic and hypercapnic gas mixture. Additional resistance was found to inhibit the ventilatory response to the chemoreceptor stimulus. The greater the ventilatory response, the more marked the inhibition. This rule is regarded as the result of interaction between chemoreceptor and mechanoreceptor afferent stimuli.

KEY WORDS: resistance to respiration; chemoreception; mechanoreception.

The pulmonary ventilation is regulated by impulses reaching the respiratory center via different afferent systems. Stimuli arriving from chemoreceptors determine the general level of ventilation to correspond to the intensity of the gas exchange of the body. Afferent impulses from proprioceptors of the respiratory muscles and mechanoreceptors of the lungs and chest wall ensure that the energy production matches the needs of the respiratory act.

The object of this investigation was to study responses of the pulmonary ventilation in man arising during interaction between increased chemoreceptor stimulation and an increased load on the respiratory system. Interaction of this sort was produced by the addition of additional resistance to respiration while the subjects inhaled gas mixtures with different partial pressures of O_2 and CO_2.

EXPERIMENTAL METHOD

Experiments were carried out on ten healthy young men wearing a mask fitted with a series of tubes to supply the required mixtures for inhalation and to record ventilation [7]. During the experiment the person remained seated and inhaled through the mask either air or one of the following mixtures: hypoxic (13.5% O_2 in N_2), hypercapnic (4% CO_2 in air), and hypoxic + hypercapnic (13.5% O_2 + 4% CO_2 in N_2). The experiments with inhalation of a particular gas mixture were repeated with each subject at least three times. The additional resistance to respiration (amounting to 20 cm water/liter/sec) was created by means of a diaphragm with a 5-mm aperture. This resistance was applied simultaneously at inspiration and expiration by means of an electromagnetic valve 10 min after the beginning of the experiment. The duration of respiration with the increased load was 30 min. In the course of the experiment, both the pulmonary ventilation and the parameters of the composition of the alveolar air and blood gases were recorded [7]. The work of inspiration, used to overcome the external resistance, was calculated from the inspiration loop. This was plotted from the spirographic record of the values of the respiratory volume and the manometric record of fluctuations of the pressure inside the mask in the course of the respiratory cycle.

EXPERIMENTAL RESULTS AND DISCUSSION

An increase in the nonelastic resistance is considered to be accompanied by an increase in the depth and decrease in the rate of respiration [5, 8, 19]. This change in the conditions is advantageous from the

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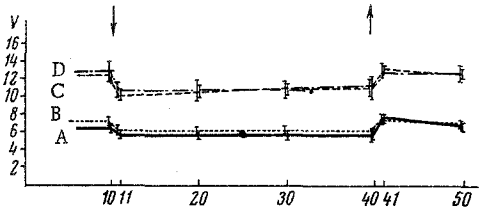

Fig. 1. Change in ventilation during application (arrow pointing downward) and removal (arrow pointing upward) of additional resistance during inhalation of air (A) or hypoxic (B), hypercapnic (C), and combined hypoxic and hypercapnic (D) mixtures. Abscissa, time (in min); ordinate, minute volume of respiration (in liters). Values of M ± m shown.

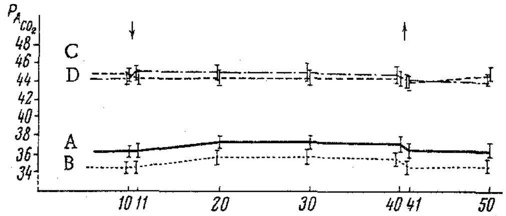

Fig. 2. Change in alveolar pCO_2 (in mm Hg) during additional resistance to respiration. Ordinate, $p_{A_{CO_2}}$ (in mm Hg). Remainder of legend as in Fig. 1.

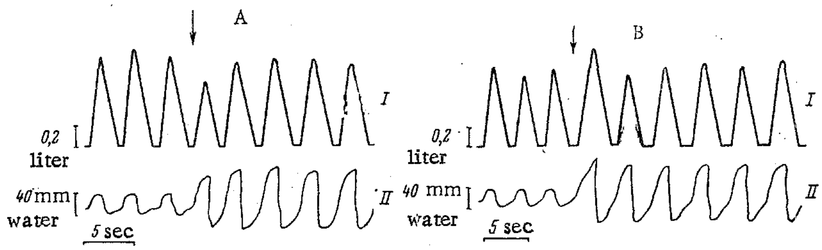

Fig. 3. Effect of additional resistance (arrow) on inhalation of hypercapnic mixture: A) first application; B) during a subsequent application of the resistance to the same subject; I) spirogram; II) record of fluctuations of pressure inside the mask.

point of view of expenditure of energy for the work of the respiratory muscles [5, 19]. In the present experiments, when the subjects inhaled air, introduction of the additional resistance caused a slowing of the rate but practically no change in the depth of respiration.

As a result, slight alveolar hypoventilation developed: the alveolar partial CO_2 pressure $p_{A_{CO_2}}$ rose ($P < 0.005$), but without any appreciable changes in the level of blood oxygenation. Removal of the additional resistance, on the other hand, led to marked hyperventilation which continued for several minutes (Figs. 1A and 2A).

The level of ventilation attained during the additional resistance to respiration was evidently the resultant of the increased load on the respiratory muscles [8] and increased activity of the respiratory center [3].

Under these conditions the source of the increased activity of the respiratory center can be assumed to be stimulation of the pulmonary mechanoreceptors of the vagus nerve [4, 12]. Some workers attach definite importance in the perception of resistance to respiration to the receptors of the chest wall [17]. Others [18], on the other hand, do not confirm this view. More recently increasing importance has been attached to the receptor function of the muscle spindles of the intercostal muscles [13, 15].

On application of the increased resistance during inhalation of the hypoxic mixture the changes in ventilation and in $p_{A_{CO_2}}$ were analogous (Figs. 1B and 2B). The blood oxygenation during inhalation of the hypoxic mixture fell to 84-86% and was not significantly changed by the additional resistance.

Additional resistance during inhalation of the hypercapnic mixture led to a much greater decrease in ventilation ($P < 0.001$), especially during the first minutes of action of the resistance. Under these circumstances the value of $p_{A_{CO_2}}$ increased significantly ($P < 0.005$; Figs. 1C and 2C).

An equally marked inhibition of ventilation ($P < 0.001$) was observed when the additional resistance was applied during inhalation of the combined hypoxic-hypercapnic mixture, i.e., during intensive action of both chemoreceptor stimuli. Here also the additional resistance to respiration led to an increase in $p_{A_{CO_2}}$ ($P < 0.005$), but it did not change the oxygenation level of the blood. Removal of the resistance during hypercapnia (and also hypercapnia combined with hypoxia) was followed by a marked increase in ventilation (Figs. 1D and 2D).

Consequently, the inhibitory effect of the additional resistance on pulmonary ventilation against the background of hypercapnia was greater than during the inhalation of air. Meanwhile hypoxia combined with hypercapnia did not change the respiratory response to mechanical loading. This could be explained by the relatively minor role of the hypoxic stimulus in the regulation of respiration compared with the hypercapnic stimulus [1]. Differences in the original volumes of ventilation during the inhalation of the various mixtures can be seen in Fig. 1.

The higher the level of ventilation under the influence of chemoreceptor stimulation, the greater the effect of the additional resistance to respiration. This was evidently due to some extent to an increase in the work of the respiratory muscles during hyperventilation. Under hypercapnic conditions the work of inspiration is a linear function of $p_{A_{CO_2}}$ [16]. The decrease in bronchial patency arising under the influence of CO_2 must also be taken into account [20]. The resistance applied in the present investigation increased the external work of inspiration by about twice ($P < 0.001$), but if the additional resistance was combined with hypercapnia the work was increased by four times.

The writers previously showed [6] that the sensitivity of ventilation to hypercapnia under the influence of additional resistance to respiration is reduced in direct proportion to its initial level. The pulmonary ventilation under those conditions is a product of two factors: activity of the respiratory center and the mechanical load on the respiratory system. These factors act in opposite directions. It will be clear that the effect of additional resistance on the volume of the pulmonary ventilation must increase with an increase in the latter.

The pattern of respiration selected by man when exposed to a combination of hypercapnia and increased resistance can be assumed to be a compromise between the need to increase the work of the ventilatory system considerably and the requirements of homeostasis: the relative hypoventilation permits a solution with the minimal possible energy expenditure [14]. However, this optimization of the respiratory act could hardly be achieved purely mechanically. The respiratory center probably integrates information arriving through the various afferent systems and leading to the formation of an adequate control signal [9]. Suprabulbar mechanisms, by means of which the system controlling respiration is capable of self-training [2], also participate in the responses to these stimuli. In the present experiments the first application of the resistance was usually accompanied by a decrease in the volume of the first inspiration against resistance, in agreement with data in the literature [10]. Subsequent applications of the same resistance not only did not induce such an action, but they frequently led to deepening of the first inspiration (Fig. 3). Judging from their verbal reports, the subjects usually felt the resistance, especially during the first few minutes after its application. This was probably due to the impulses from the muscle proprioceptors mentioned above. Some workers [11] ascribe great importance to this "awareness" in the regulation of respiration in man during exposure to increased loads.

Responses of human ventilation to the combined effect of added resistance to respiration and changes in the partial pressures of the respiratory gases are thus the result, first, of the increased load on the respiratory muscle and second, interaction between afferent stimuli of different modalities directed to the respiratory center in conjunction with the mechanisms of cortical control of respiration.

LITERATURE CITED

1. I. S. Breslav, A. G. Zhironkin, V. N. Salazkin, et al., Fiziol. Zh. SSSR, No. 11, 1749 (1972).
2. A. Z. Kolchinskaya, in: The Function of External Respiration in a Modified Atmosphere [in Russian], Leningrad (1971), p. 53.
3. A. M. Kulik and L. N. Kondrat'eva, Kosmich. Biol. i Med., No. 5, 29 (1972).
4. V. S. Raevskii, S. V. Tolova, V. V. Antipov, et al., Fiziol. Zh. SSSR, No. 11, 1335 (1968).
5. Ya. I. Trumpaits and S. L. Kaminskii, in: Proceedings of the Fifth All-Union Conference on Work Physiology [in Russian], Moscow (1967), p. 296.
6. R. I. Khvalibova, Fiziol. Zh. SSSR, No. 4, 624 (1974).
7. A. M. Shmeleva, I. S. Breslav, and B. N. Volkov, Fiziol. Zh. SSSR. No. 7. 1139 (1973).

8. L. Beneken, H. Kleinsorg, and K. Kochsick, Klin. Wschr., 39, 1049 (1961).
9. E. J. M. Campbell, C. J. Dickinson, et al., Clin. Sci., 21, 309 (1961).
10. F. N. Cragi, W. V. Blevins, and E. G. Cummings, J. Appl. Physiol., 29, 847 (1970).
11. Z. Dziewanowska-Kunnert, Acta Neurobiol. Exp., 32, 773 (1972).
12. C. von Euler, in: Breathlessness, London (1966), p. 19.
13. R. Gilbert, J. H. Auchincloss, et al., Resp. Physiol., 13, 238 (1971).
14. R. Granit, The Basis of Motor Control, London (1970).
15. J. Milic-Emili and J. M. Tyler, J. Appl. Physiol., 18, 497 (1963).
16. J. Newson Davis, J. Physiol. (London), 179, 25 (1965).
17. M. G. M. Noble, H. L. Frankel, et al., Clin. Sci., 41, 285 (1971).
18. A. B. Otis, W. O. Fenn, and H. Rahn, J. Appl. Physiol., 2, 592 (1950).
19. J. R. Rodart and R. E. Hyatt, Resp. Physiol., 17, 135 (1973).