Control experiments with random stimulation of the embryos showed that under these circumstances the periods described above were absent and there was no decrease in the number of stimuli.

The experimental results thus indicate specific oriented transformations of movements toward the end of embryogenesis in regimes of control oriented in different directions. The single adaptive effect (minimization of stimulating influences) is produced by structural and temporal modifications of the biorhythm of motor activity with a selective enhancement of components not reinforced by adverse (nociceptive) stimulation. This points to the role of endogenous biorhythms as a mechanism of optimization of relations between the organism and its environment [3], which are actively incorporated into adaptive control before the end of embryogenesis in chicks.

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INTERACTION BETWEEN HYPERCAPNIC AND HYPOXIC RESPIRATORY DRIVE DURING MUSCULAR EXERTION

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During the performance of graded muscular exertion against the background of controlled hypercapnia, hypoxia, hyperoxia, and their combinations, the dynamics of the pulmonary ventilation ($\dot{V}$) and the composition of the alveolar gas ($p_a CO_2$, $p_a O_2$) were investigated in 12 healthy men. The respiratory response was assessed from the absolute values of ventilation at a given value of $p_a CO_2$ and from its increase per mm Hg increase in $p_a CO_2$ ($\Delta\dot{V}/\Delta p_a CO_2$) at rest and on transition to and with establishment of stable conditions of exertion. The respiratory response at the beginning of exertion was accompanied by an upward shift and an increase in the slope of the $\Delta\dot{V}/\Delta p_a CO_2$ line, independent of the magnitude of exertion. These changes point to multiplicative ineraction between neurogenic and hypercapnic stimuli with the commencement of exertion. In the steady state of exertion a significant role of the hypoxic stimulus was discovered: During hypoxemia the $\Delta\dot{V}/\Delta p_a CO_2$ line was found to be appreciably shifted upward, especially during intensive exertion. This proves that positive interaction between hypercapnic and hypoxic stimuli is potentiated during exertion.

KEY WORDS: regulation of respiration; chemoreceptors; proprioceptors; interaction between respiratory drives; muscular activity.

Complex interaction between the stimuli controlling respiration during muscular activity is still largely unexplained. The importance of chemoreceptive stimuli in the genesis of the neurogenic components of the ventilatory on-response to exertion has recently been demonstrated [1, 5].

The functions of the chemoreceptor apparatus are generally assessed by the response of the pulmonary ventilation to a hypercapnic stimulus. This response is usually measured during rebreathing with CO_2 accumulation. However, this test is difficult to carry out during phys-

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TABLE 1. Relationship between Pulmonary Ventilation and p_a CO_2 during Performance of Measured Work under Different Conditions

Conditions	Exertion, kg·m/min		
	0	300	600
	P_ACO_2, liters/min · mm Hg		
Normoxia			
rest	1,32	1,32	1,32
beginning of exertion	1,56*	1,56*	2,10*
steady state of exertion	2,43*	3,12*	3,09*
Hyperoxia			
rest	1,25	1,25	1,25
beginning of exertion	1,70*	1,79*	1,78*
steady state of exertion	2,25*	2,78*	2,87*
Hypoxia			
rest	1,11	1,11	1,11
beginning of exertion	1,43*	1,37*	1,59*
steady state of exertion	1,74*	2,08*	1,56*

*Differences from resting level significant ($P < 0.05$).

ical exertion, and this is one reason why there is no precise information on the role of chemoreceptive stimuli in the regulation of respiration during muscular activity. The problem is complicated by the participation of the hypoxic factor, and both chemoreceptive stimuli — hypercapnic and hypoxic — exhibit positive interaction within certain limits [6, 8]. Moreover, the contribution of these stimuli to the various phases of muscular activity may vary.

The object of the present investigation was to study the following problems: Does the response of the pulmonary ventilation to a hypercapnic stimulus vary during physical exertion; what is the effect of a hypoxic stimulus on this response; is the role of chemoreceptor stimuli the same during exertion under transitional and steady-state conditions?

For this purpose the pulmonary ventilation was compared the magnitudes of acting stimuli — hypercapnic and hypoxic — at rest, at the time of commencing graded muscular exertion, and after establishment of the steady state of exertion. The investigation was carried out during inhalation of gas mixtures with different concentrations of CO_2 and O_2.

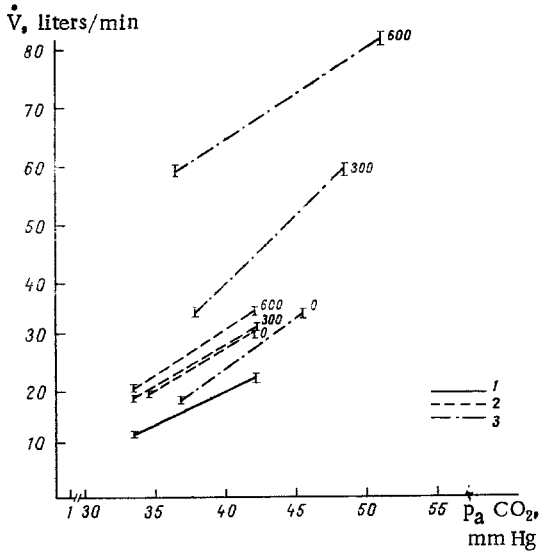

Fig. 1. Pulmonary ventilation ($\dot{V}$) as a function of p_a CO_2 during exertion at different intensities and under normoxic conditions (numbers on graph show power of exertion in kg·m/min). Here and in Figs. 2 and 3: solid line) rest, dashed line) beginning of exertion, dot-dash line) steady state of exertion.

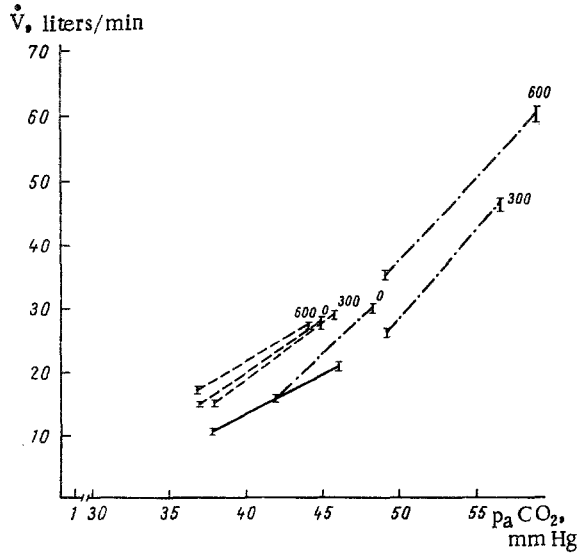

Fig. 2. Pulmonary ventilation ($\dot{V}$) as a function of $p_a CO_2$ during exertion at different intensities under hyperoxic conditions (figures on graph show power of exertion in kg · m/min).

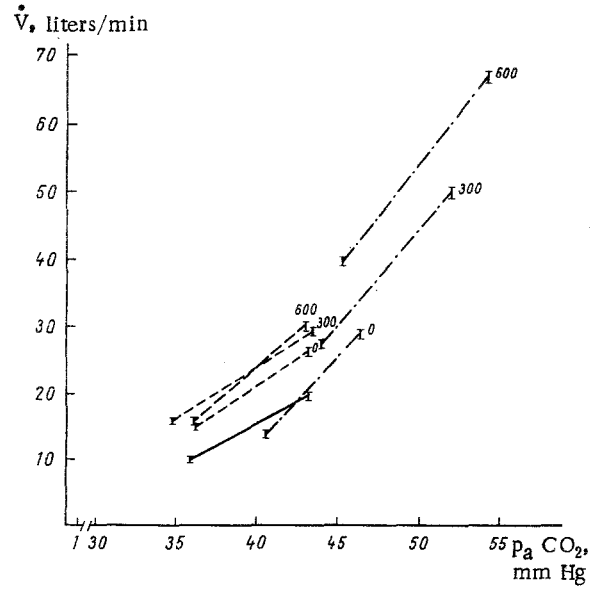

Fig. 3. Pulmonary ventilation ($\dot{V}$) as a function of $p_a CO_2$ during exertion at different intensities under hypoxic conditions (numbers on graph show power of exertion in kg · m/min).

EXPERIMENTAL METHOD

During the investigation 20 healthy young men breathed through a mask air, pure oxygen, or the following mixtures: 4% CO_2 in air or oxygen; 30% O_2 in nitrogen; 4% CO_2 + 13% O_2 in nitrogen. Muscular work was performed on a bicycle ergometer. The power of exertion was 0 ("freewheeling"), 300 and 600 kg·m/min, during pedaling at a speed of 60 rpm. The pulmonary ventilation was recorded on a modified spirograph. As indicators of chemoreceptive stimuli, the partial pressures of the gases in the alveolar air ($p_a CO_2$, $p_a O_2$) were recorded continuously by means of the MKh 6202 mass spectrometer.

Depending on the levels of $p_a O_2$ the experiments were divided into three series: normoxic (100-130 mm Hg), hyperoxic (200 mm Hg or more), and hypoxic (50-70 mm Hg); in each series there were some experiments which were carried out under normoxic and hypercapnic conditions. Accordingly, within the same series, it was possible to compare the values of the pulmonary ventilation ($\dot{V}$) at different values of $p_a CO_2$ at rest and during exertion of different intensities for the transitional (the first 20 sec) and the steady (5th minute of exertion) states.

The respiratory response to the hypercapnic stimulus was assessed from the absolute values of the ventilation at given values of $p_a CO_2$ and the increase in ventilation per mm Hg increase in $p_a CO_2$ ($\Delta\dot{V}/\Delta p_a CO_2$), determined by linear regression. Calculations were carried out on the M-3040 computer.

EXPERIMENTAL RESULTS

Under normoxic conditions (Fig. 1; Table 1) the beginning of exertion was accompanied by an upward shift and an increased slope of the $\Delta\dot{V}/\Delta p_a CO_2$ line which was independent of the intensity of exertion.

During steady-state exertion the response of respiration to the hypercapnic stimulus, to judge from the graph, increased still more. However, it must be recalled that the $\Delta\dot{V}/\Delta p_a CO_2$ lines on this graph were within different $p_a CO_2$ limits for the resting, transitional, and steady states of exertion; in the last case, moreover, $p_a CO_2$ was increased, evidently on account of an increase in metabolism. Yet the increase in ventilation per mm Hg pCO_2 is known to be greater at relatively high values of $p_a CO_2$ than low [6]. In the present case this could be the cause of the increase slope of the $\Delta\dot{V}/\Delta p_a CO_2$ line. At the same time, it must be pointed out that the magnitude of the shift of the $\Delta\dot{V}/\Delta p_a CO_2$ line upward clearly depended on the power of exertion. Under steady-state conditions of "zero" work this line had a tendency to revert to the resting level.

During muscular exertion under hyperoxic conditions (Fig. 2; Table 1) the parameters of the ventilatory response to CO_2 differed only a little from those described above. Compared with data obtained under normoxic conditions, the only noticeable difference was a smaller upward shift of the $\Delta\dot{V}/\Delta p_a CO_2$ line, despite the greater increase in $p_a CO_2$.

Against the background of hypoxemia (Fig. 3; Table 1) the beginning of exertion, just as in normoxia, increased the slope of the $\Delta\dot{V}/\Delta p_a CO_2$ line relative to its background position. By contrast, the respiratory response to CO_2 during steady-state exertion was much more dependent on the magnitude of the load: The greater the intensity of the work done, the greater the upward shift of the $\Delta\dot{V}/\Delta p_a CO_2$ line.

It can tentatively be suggested that the neurogenic stimulus activated at the beginning of exertion [2-4, 6, 7] interacts with the hypercapnic stimulus by the multiplicative principle: The two stimuli potentiate one another, as shown by upward displacement of the $\Delta\dot{V}/\Delta p_a CO_2$ line. The neurogenic stimulus probably owes its origin chiefly to impulses from proprioceptors of the contracting muscles [7], for it is found even at "zero" exertion. Meanwhile it is important to emphasize that this factor causes an increase in pulmonary ventilation not by itself, but only through chemoreceptive stimulation of respiration. This is shown by disappearance of the fast phase of the ventilatory on-response to exertion after hyperventilation with oxygen, i.e., in the absence of hypoxic and hypercapnic stimuli [1].

It is a different matter with regulation of respiration during steady-state conditions of muscular activity, when an increased ventilatory response to CO_2 also is observed: In this case the increase depends on the power of the working load. Under these conditions it may be that besides changes in pCO_2 and pO_2, some other humoral factor of metabolic origin also exerts its influence [6]. Arterial blood analyses in fact revealed metabolic acidosis during muscular exertion under normoxic and hyperoxic conditions. During hypoxia, however, when the greatest respiratory response was observed to hypercapnia, the metabolic acidosis was in fact compensated by the development of respiratory alkalosis, and as a result the true pH of the arterial blood remained within normal limits.

The increase in ventilation observed at comparable values of $p_a CO_2$ can be explained by potentiation of positive interaction between the two chemoreceptive stimuli. During muscular activity the effect of the hypoxic stimulus on ventilation is evidently increased [9] and it has a more marked potentiating action on the effect of the hypercapnic stimulus.

The relationship between the mechanisms of regulation of respiration thus differs significantly in the transitional and steady states of muscular activity.

At the commencement of exertion the humoral stimuli provide what is evidently the essential background for the action of the neurogenic factor triggering the ventilatory response. Hypercapnic and hypoxic stimuli in the transitional phase potentiate the effect of this factor, but positive interaction between them remains the same as at rest.

During steady-state muscular activity, however, hypoxic—hypercapnic interaction is considerably potentiated and the more so the greater the intensity of work.

Potentiation of both chemoreceptor stimuli is an inevitable consequence of the increased level of metabolism. The increased sensitivity of the apparatus controlling respiration to this combination of stimuli must evidently facilitate the maintenance of pulmonary ventilation at a level appropriate to the power of exertion.

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