RESPONSE TO MONITORED HYPERCAPNIA DURING MUSCULAR WORK

I. S. Breslav, A. M. Shmeleva,
and S. M. Sidikov

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The problem of interaction between mechanisms regulating respiration during muscular activity is still far from being solved. Data published recently [3, 4, 6, 9] suggest that during physical exertion an essential role in the control of the pulmonary ventilation is played, just as at rest, by chemoreceptor stimuli. Admittedly, the effect of these stimuli when the load is applied is masked by the rapid rise in ventilation due evidently to cortical control and impulsation from receptors of the working muscles [5, 7]. The contribution of the "chemical" regulation of respiration is detected much more easily in the steady-state period of work, when ventilation is established to correspond to the increased energy expenditure of the body.

However, the high level of the pulmonary ventilation during muscular work cannot easily be entirely ascribed to the influence of humoral changes in the body, which often cannot be detected at all. Attempts have been made to explain this state of affairs either by a sharp increase in sensitivity of the regulatory apparatus of respiration to chemoreceptor stimuli — both hypercapnic and hypoxic — or by interaction between these stimuli with "nonchemical," "neurogenic" factors (see the survey in [2]).

The elucidation of this problem is complicated by the difficulty of direct determination of responses of respiration to chemoreceptor stimuli during physical work. The most accurate method of measuring the ventilation response to the leading, hypercapnic stimulus is to determine the increase in the pulmonary ventilation during rebreathing, with gradual accumulation of CO_2 excreted by the experimental subject or animal in the lungs—bag system. However, during muscular exertion this method may not give comparable results, because a sharp rise in CO_2 production leads to a more rapid increase in its concentration in the system.

To overcome this difficulty the writers developed a method of monitored alveolar hypercapnia, by means of which a curve of the response of respiration to the stimulus can be obtained with a rate of rise that is programmed beforehand and is independent of the physiological state of the organism [1]. By using this method an attempt was made to assess how the response of human respiration to a measured hypercapnic stimulus changes under the influence of physical work.

EXPERIMENTAL METHOD

Four healthy young men performed work of different power on a bicycle ergometer: "zero" (freewheeling), and 50 and 100 W. The subject breathed air through a mask with low resistance of its valves. By means of a modified spirometric system the respiratory minute volume ($\dot{V}$), the duration of the respiratory cycle (T), and the tidal volume (V_T) were recorded. The partial pressure of CO_2 in the alveolar air (pCO_2) was recorded on a capnograph (Godart).

The response to monitored hypercapnia was determined at rest and during exertion (beginning in the 5th minute of work). The method of testing, similar to that described previously [1], consisted in creating a uniform increase in pCO_2 from 50 to 63 mm Hg, by controlling the composition of the inspired mixture, in the course of 2.5 min. The response

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TABLE 1. Parameters of Response of Ventilation to Controlled Alveolar Hypercapnia at Rest and during Work

Subject	S, liters/min/mm Hg		B, mm Hg	
	R	W	R	W
VB	2,0	1,8	34,4	22,3
SG	2,4	1,6	44,5	28,8
LK	2,2	2,3	40,9	33,2
SR	4,0	4,0	39,0	24,3
Mean	2,6	2,4	39,7	27,2*

*Changes significant compared with resting conditions ($P < 0.01$).

Legend. Here and in Table 2: R) rest, W) during work of 50 W. Mean values calculated for 3-6 experiments of the same kind given for each subject.

TABLE 2. Parameters of Respiration at Rest and during Work

Subject	$\dot{V}$, liters/min		T, sec		V_T, liters	
	R	W	R	W	R	W
Before beginning of testing						
VB	10,1	31,2	3,5	3,5	0,6	1,8
SG	7,3	30,7	3,5	2,7	0,4	1,3
LK	10,4	28,4	3,6	2,6	0,6	1,2
SR	9,1	33,4	4,3	3,3	0,6	1,8
Mean	9,2	30,9*	3,7	3,0	0,6	1,5*
At pCO_2 = 55 mm Hg						
VB	40,6	54,4	3,1	2,8	2,0	2,6
SG	24,7	42,1	2,9	2,5	1,1	1,9
LK	31,8	48,9	2,8	2,3	1,4	1,8
SR	63,3	121,3	2,7	1,5	2,7	3,5
Mean	40,1	66,7*	2,9	2,3*	1,8	2,4*

*The same as in Table 1.

was evaluated by the linear regression method in terms of the increase in ventilation per mm Hg increase in pCO_2 (the slope of the regression line, or parameter S), and of the value of pCO_2 at the point of intersection of the extrapolated regression line with the "zero" ventilation axis (the parameter B) in accordance with the known equation:

$$\dot{V} = S\,(p_{CO_2} - B).$$

The absolute value of these parameters before the beginning of testing (i.e., when pCO_2 was uncontrolled) and during controlled hypercapnia when pCO_2 was 55 mm Hg, also was taken into account.

Calculations were done on the M-3040 computer.

EXPERIMENTAL RESULTS

According to Table 1 and Fig. 1, muscular work caused no regular changes in the slope of the curve reflecting the response of ventilation to CO_2 (the parameter S). Consequently, the sensitivity of the system controlling respiration to the hypercapnic stimulus was unchanged.

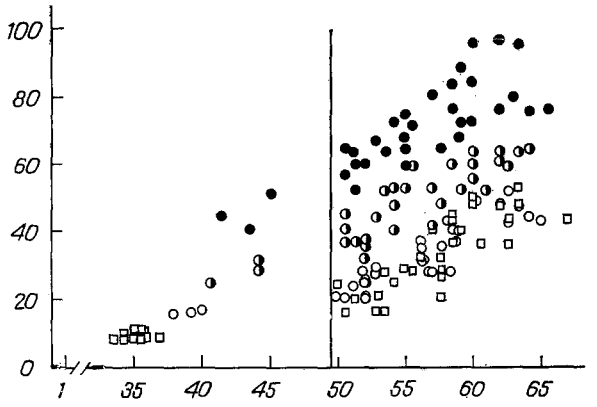

Fig. 1. Dependence of pulmonary ventilation on pCO_2 during controlled hypercapnia at rest and during graded muscular exertion (subject L. K.). Abscissa, pCO_2 (in mm Hg); ordinate, $\dot{V}$ (in liters/min). Squares denote rest, circles — work; empty circles — "zero," half-filled — 50 W, filled — 100 W.

Meanwhile, in all subjects during work B shifted to lower values of pCO_2 than at rest. This led to a shift of the lines reflecting the dependence of pulmonary ventilation on pCO_2 upward and to the left; compared with resting conditions, this shift gradually increased with an increase in the power of work, and it was almost absent at "zero" load (Fig. 1). As a result, a higher value of ventilation than at rest corresponded to all given values of the hypercapnic stimulus during work (Table 2; Fig. 1). This "working" increase took place on account of a predominant increase in respiratory volume; the action of hypercapnia, however, also was reflected in considerable shortening and, consequently, quickening of the respiratory cycles (Table 2).

The results indicate that during muscular activity the hypercapnic stimulus to respiration is joined by an additional stimulus, proportional to the size of the load. If this is true, the "working" ventilation will be described by the sum:

$$V = S\,(pCO_2 - B) + kA,$$

where A is the power of work done and k is a coefficient of nonproportionality.

The "working" stimulus is evidently connected to some degree with the hypoxic factor: During work the response of ventilation to CO_2 in hypoxia rises sharply, whereas in hyperoxia it virtually disappears [4]. On the other hand, the stimulus we are considering depends on the magnitude of the physical load. In this case interaction probably takes place between hypercapnic and hypoxic factors and a certain specific factor directly responsible for muscle contractions.

It was postulated on the basis of an investigation [8], in which the potentiating action of hypoxemia on the increase in ventilation in man during work was confirmed, that under the influence of hypoxia receptors of working muscles are sensitized, and the impulsation of these receptors in turn somehow potentiates hypoxic stimulation of arterial chemoreceptors. However, in another investigation [9] conducted on dogs, the response of the ventilation to "work" evoked by electrical stimulation of the hind limbs was largely preserved after reflex influences had been blocked not only from the "working" limbs themselves (which were denervated), but also from arterial and medullary chemoreceptors. No significant changes in the gas composition or pH of the arterial blood were observed under these circumstances. During muscular exertion, respiration is thus regulated by an unknown humoral agent, which acts through unknown receptors.

Consequently, neither the nature nor the point of application of the hypothetical "working" stimulus is yet known. However, the investigation described above shows that in the steady-state period of muscular activity this stimulus can interact by an additive mechanism with the hypercapnic stimulus, which is the dominant factor in the regulation of respiration.

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SECRETORY AND EXCRETORY FUNCTIONS OF THE STOMACH AFTER REMOVAL OF THE SUBMANDIBULAR SALIVARY GLANDS

V. N. Vasil'ev and V. D. Sukhodolo

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The problem of functional connections between the salivary glands and organs of the gastrointestinal tract is an important one in modern gastroenterology [8, 11, 15]. There is evidence of changes in the secretory and motor activity of the digestive organs after total sialadenectomy, and also in cases of loss of the mixed saliva and its introduction into the digestive tract [5, 6, 11-14]. It has accordingly been stated that the salivary glands perform a purely digestive function [2, 10] and, through the production of active kallikrein and other biologically active substances, they play a role in the development of working hyperemia of the digestive organs and inhibition of gastric secretion [8, 9].

The object of this investigation was to study the main components of the secretory and excretory functions of the stomach in rats after removal of the submandibular salivary glands.

EXPERIMENTAL METHOD

Experiments were carried out on 103 noninbred albino rats weighing 200-280 g. The fasting secretion of gastric juice was studied by Shay's method [13]. The secretion was collected for 3 h. The secretory and excretory functions of the stomach were studied in parallel tests on 47 control rats and 49 rats on the 7th, 14th, 21st, 28th, and 42nd days after preliminary extirpation of the submandibular salivary glands, and also on eight animals on the 7th day after a mock sialadenectomy. The state of secretion of the glands was assessed from the total volume of the secretion, its proteolytic activity [1], and the absolute hydrogen ion secretion in unit time [3]. To determine the excretory function of the gastric glands the method of gastrochromoscopy was used, with quantitative estimation of neutral red [4]. The dye was injected intravenously as a 1% solution in a dose of 2 mg/kg. To obtain additional data for interpretation of possible changes in the excretory function of the stomach, in parallel experiments the urea and sugar concentrations in the blood and gastric juice of the experimental animals were studied [7]. The numerical results were subjected to statistical analysis by Student's t-test. Differences were considered to be significant at the $P \leq 0.05$ level.

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