ROLE OF CHEMORECEPTOR STIMULI IN DETERMINING THE RATE OF ACTIVATION AND INACTIVATION OF THE RESPIRATORY RESPONSE TO EXERCISE

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It is generally accepted that the respiratory response to work is activated and inactivated through the action of neurogenic factors connected with physical exertion – cortical and proprioceptive [4, 5]. Meanwhile, humoral stimuli, hypercapnic and hypoxic, mediated through medullary and arterial chemoreceptors, also participate in the regulation of respiration during muscular activity. The role of these chemoreceptors in the control of pulmonary ventilation in the different phases of work has not yet been adequately studied.

The writers showed previously [1, 2] that in the steady-state period of exercise the sensitivity of the respiratory control apparatus to a combination of hypoxic and hypercapnic stimuli is appreciably increased. Moreover, it has been shown that these stimuli have a significant effect also on the intensification of pulmonary ventilation at the beginning of work, i.e., on the phase which (like the decrease in ventilation at the end of the work) is generally attributed entirely to the "nonchemical" factors mentioned above and which is called the rapid neurogenic component of the respiratory response to exercise.

The main aim of the present investigation was to assess the contribution made by chemoreceptor regulation in the transitional phases of "working hyperpnea." For this purpose, under conditions of hypercapnic and hypoxic stimulation of different intensity, during work, the magnitude and rate of rise and fall of the pulmonary ventilation respectively were determined at the beginning and end of exercise.

EXPERIMENTAL METHOD

The pulmonary ventilation was recorded in 12 healthy men aged 22-35 years, breathing through a mask in the sitting position, on a modified spirograph. After a 5-min background period of rest, the subject did work for 5 min on a bicycle ergometer with a power of 50 or 100 W, turning the pedals at a speed of 60 rpm. The work began and ended in response to an illuminated signal. During the 2 min after the beginning of exercise and the same period after its end, and also at the 5th minute all indices were recorded for periods of 10 sec. The half-reaction time, during which ventilation increased (at the beginning of work) and decreased (at the end of work) to a value equal to half the difference between the background (resting) level and the steady-state period of exercise (5th minute) and, correspondingly, between the steady-state periods of exercise and of recovery, was calculated. By dividing these values, i.e., half the increase and half the decrease in ventilation, by the half-reaction time at the beginning and end of exercise, indices were obtained for the rate of activation and inactivation of the ventilatory response. Experiments were carried out on subjects breating air (control) and various gas mixtures; hypercapnic (4% CO_2 in air), hypoxic (13% O_2 in nitrogen), hypercapnic-hypoxic (4% CO_2+13% O_2 in nitrogen); hyperoxic (100% O_2), and hypercapnic-hyperoxic (4% CO_2 in oxygen) or after preliminary (for 30 sec before the beginning of work) voluntary hyperventilation with air or oxygen. The relative values of the hypercapnic and hypoxic stimuli were assessed from the partial pressures of the gases in the alveolar air ($pACO_2$ and pAO_2), which were recorded by means of the MKh 6202 mass spectrometer. The investigations during work of different power and in respiratory mixtures of different composition were alternated in randomized order.

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TABLE 1. Parameters of Response of Pulmonary Ventilation to Exercise under Conditions of Altered Chemoreceptor Stimulation of Respiration (M ± m)

Load, W	Composition of ventilatory mixture, %		n	$pACO_2$ mm, Hg	pAO_2, mm Hg	Pulmonary ventilation, liters·min^{-1}					Mean half-reaction time, sec		Rate index, ml·min^{-1}·sec^{-1}	
						at rest	exercise for 5 min	recovery for 5 min	half-reaction					
	O_2	CO_2							activation	inactivation	activation	inactivation	activation	inactivation
50	21 (control)	0	120	35,6±0,1	106,8±0,3	10,2±0,1	27,2±0,5	10,8±0,1	8,5±0,3	8,2±0,2	39,6	37,1	215±8	221±6
	13	0	36	33,1±0,3	58,1±0,3	10,6±0,1	34,4±0,5	11,9±0,1	11,9±0,3†	11,2±0,3†	36,4	34,1	327±9†	330±10†
	21	4	36	43,8±0,2	131,9±0,2	20,2±0,4	52,1±0,7	23,7±0,4	16,0±0,5†	14,2±0,4†	44,3	43,6	360±10†	327±10†
	13	4	36	42,4±0,2	75,7±0,2	19,2±0,4	57,1±0,8	22,8±0,5	16,9±0,8†	17,1±0,5†	39,8	41,3	425±19†	415±13†
	96	4	36	45,9±0,2	>200	20,1±0,4	45,7±0,8	23,3±0,5	12,8±0,5	11,2±0,4	60,6	49,2	211±9	228±8
	100	0	36	37,7±0,2	>200	10,1±0,1	25,5±0,5	10,8±0,1	7,7±0,3	7,3±0,3	44,5	39,3	173±7	187±7
	21 (hyperventilation)	—	36	36,0±0,2	106,5±0,2	10,7±0,1	28,3±0,3	11,2±0,2	8,8±0,4	8,5±0,3	78,3	39,4	113±5†	217±7
	100 (hyperventilation)	—	36	36,7±0,4	>200	11,3±0,1	25,2±0,4	11,3±0,1	6,9±0,2†	6,9±0,2†	105,0	50,1	63±2†	138±5†
100	21 (control)	0	120	36,4±0,1	106,2±0,3	9,6±0,1	39,5±0,6	11,3±0,2	14,9±0,4	14,1±0,3	49,0	47,6	305±7	295±7
	13	0	36	33,3±0,3	57,1±0,3	10,6±0,1	56,2±1,0	13,7±0,2	22,8±0,8†	21,2±0,6†	53,2	41,0	429±15†	518±15†
	21	4	36	43,4±0,2	131,8±0,1	20,1±0,3	67,3±1,1	26,8±0,6	23,6±0,4†	20,3±0,8†	55,0	62,2	429±8†	326±12
	13	4	36	42,5±0,2	77,0±0,2	21,2±0,4	79,4±1,4	27,8±0,6	29,1±0,6†	25,8±1,2†	49,4	48,6	589±12†	530±24†
	96	4	36	44,1±0,2	>200	21,6±0,4	60,1±0,9	26,6±0,5	19,2±0,4	16,7±0,5	65,4	63,8	294±7	262±8
	100	0	36	37,2±0,2	>200	10,3±0,1	37,3±0,8	12,4±0,2	13,5±0,4*	12,4±0,5†	62,4	61,0	216±7*	203±8*
	21 (hyperventilation)	—	36	35,8±0,2	107,1±0,2	10,2±0,1	39,3±0,6	11,4±0,1	14,5±0,4†	13,8±0,4	75,2	51,4	193±6†	269±8
	100 (hyperventilation)	—	36	37,1±0,4	>200	10,4±0,1	34,5±0,8	12,0±0,2	12,0±0,4†	11,2±0,4†	100,0	57,1	120±4†	197±7†

Legend. *P < 0.05, †P < 0.001 compared with control.

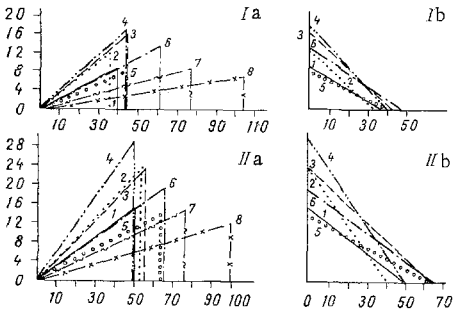

Fig. 1. Magnitude and time of ventilatory half-response to starting and stopping exercise during chemoreceptor stimuli of different intensities. I) Load 50 W; II) load 100 W. a) Start of exercise, b) end of exercise. Abscissa, half-reaction time (in sec); ordinate, magnitude of ventilatory half-response (in litres/min). 1) Inhalation of air (control), 2) of 13% O_2 in nitrogen, 3) of 4% CO_2 in air, 4) of 13% O_2 + 4% CO_2 in nitrogen, 5) 100% O_2, 6) 4% CO_2 in oxygen, 7) inhalation of air after preliminary hyperventilation before beginning of exercise, 8) of 100% O_2 after preliminary hyperventilation.

EXPERIMENTAL RESULTS

Comparison of the parameters of the ventilatory response to exercise during inhalation of different mixtures (Table 1; Fig. 1) shows that the magnitude of the response in general increased with an increase in the intensity of chemoreceptor stimulation and was maximal (almost doubled) during a combination of hypercapnea and hypoxia. Under ordinary conditions, the hypercapnic factor is known to have a relatively stronger influence on respiration, but it was noted that with an increase in the load the contribution of the hyperoxic stimulus increased [3]. In fact, during exercise with a power of 100 W inhalation of a mixture of 13% O_2 in nitrogen increased the increase in ventilation to the same degree as inhalation of a mixture of 4% CO_2 in air. Stopping the hypoxic stimulus by inhalation of oxygen, on the other hand, in most cases reduced the ventilatory response to work. This response was weakened still more after preliminary hyperventilation with oxygen, which temporarily abolished both chemoreceptor stimuli.

Let us now examine the index of the rate of activation of the ventilatory response at the beginning of exercise (Table 1, Fig. 1). This index depended even more than the magnitude of the response on humoral factors. Attention is drawn to the particular features of the influence of hypercapnic and hypoxic factors. Whereas during exercise with an intensity of 50 W hypercapnea increased the rate of activation almost as much as a combination of hyperocapnea with hypoxia, and the effect of isolated hypoxia was somewhat weaker, during exercise with an intensity of 100 W the action of the hypoxic stimulus increased relatively.

Against the background of hyperoxia, inhalation of CO_2 in general did not affect the rate of activation of the ventilatory response. Inhalation of pure oxygen caused this index to fall, and the decrease was very considerable with a load of 100 W. The role of the hypoxic stimulus in the transitional state of muscular activity was thus even more important than in the steady state. After hyperventilation with air, and in particular, with oxygen marked slowing of the increase in pulmonary ventilation at the beginning of exercise was observed.

The index of the rate of inactivation of the ventilatory response after removal of the load showed similar correlation with chemoreceptor stimulation of respiration. The stronger the stimuli, the faster the pulmonary ventilation diminished; all that need be mentioned is that hypoxia accelerated inactivation of the response to a greater degree than hypercapnea. Inhalation of oxygen, on the other hand, especially after a preliminary hyperventilation, lowered the rate index of inactivation.

These results are evidence that a hypercapnic stimulus can both strengthen and accelerate the response of respiration to muscular activity. The action of this stimulus is known to be mediated through both arterial and medullary chemoreceptors. Participation of the latter can explain the fact that the effect of preliminary hyperventilation before exercise was exerted at the level of the respiratory minute volume at the 5th minute

of exercise, whereas alveolar hypocapnea disappeared as early as 40 sec after the end of hyperventilation: This was evidently due to the slow change in pCO_2 in the medullary chemosensitive zones, as a result of which the hypercapnic stimulus was weakened for such a long time.

As regards the fast-reacting arterial chemoreceptors, it was evidently their excitation which affects the rate of activation and inactivation of "working hyperpnea." When the hypercapnic stimulus acted against the background of hyperoxia – and in hyperoxia the arterial chemoreceptors lose their sensitivity to CO_2 and the latter acts only through medullary chemoreceptors – the indices of the rate of activation and inactivation of the ventilatory response to exercise were practically the same as in the control (inhalation of air), although the increase in ventilation induced by work in this case was greater. The suggestion that arterial chemoreceptors play an important role in the regulation of respiration in transitional phases of muscular activity is confirmed by the fact that removal of the carotid bodies in man, although not significantly changing the levels of ventilation during moderate exertion, delays the increase in ventilation at the beginning of work [6].

The results obtained in the present experiments when the intensity of the hypoxic stimulus was changed (and this stimulus is known to act through these receptors exclusively), are in agreement with the facts described above. The hypoxic factor was particularly important for the rapid development of the ventilatory response at the beginning of exertion and when the ventilation returned to the resting level after the end of exertion.

The great importance of the hypoxic stimulus for rapid reduction of pulmonary ventilation to correspond to the energy demands of the body is evidently due to the extremely small reserves of oxygen in the blood, necessitating rapid responses of respiration (and, of course, of the circulation), which maintain an adequate supply of oxygen to the working muscles.

Hypoxic stimulation of respiration thus potentiates the action of the above-mentioned neurogenic factors triggering "working hyperpnea." The mechanism of this action, however, is not yet clear.

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