ABILITY OF MAN TO MAINTAIN A STEADY RESPIRATION PATTERN WHILE INHALING DIFFERENT GAS MIXTURES

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Interaction between "involuntary" and "voluntary" factors in regulation of respiration in young adults was studied. On receiving a verbal command the subjects maintained a steady pattern (rate and depth) of respiratory movements not only while breathing air, but also while inhaling hypoxic and hypercapnic mixtures. Involuntary disturbance of the fixed pattern of respiration occurred if the decrease in oxygen concentration (to 7%) or increase in carbon dioxide concentration (to 4%) exceeded certain limits, depending on the intensity of the ventilatory response of individual subjects to these mixtures and also on the assigned level of pulmonary ventilation.

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In response to a verbal command, a human subject can maintain an assigned frequency and depth of his respiration [5, 6, 8]. The ability to control the pattern of respiration voluntarily is naturally restricted by the demands of maintaining the gas exchange of the organism [2, 3]. These demands are expressed through reflex and humoral stimuli.

Interaction between "involuntary" and "voluntary" factors in regulation of respiration has received inadequate study. Attempts have been made to investigate this problem by combining a fixed pattern of

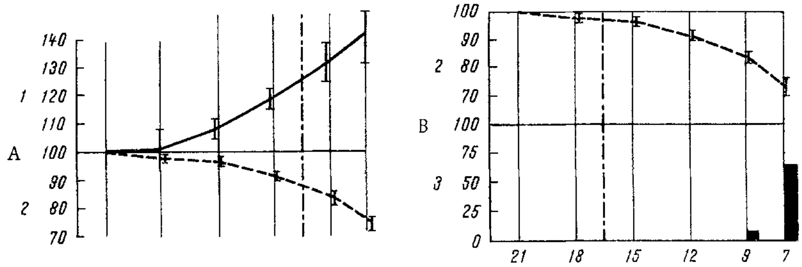

Fig. 1. Response of human subject to hypoxic mixture during free (A) and fixed (B) patterns of respiration. Abscissa, percentage of oxygen in inspired mixtures. Mixtures shown on the right of the vertical broken line (dots and dashes) were avoided by more than two-thirds of subjects. Ordinate: 1) minute volume of respiration; 2) oxygen saturation of blood (percent of level during inhalation of air, vertical lines show standard errors of means); 3) number of cases of disturbance of assigned respiration pattern—respiratory volume exceeded (percent of total number of experiments).

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respiration, established in response to a verbal command, with changes in the composition of the inspired gas mixtures.

EXPERIMENTAL METHOD

Each series of experiments was carried out on 12 healthy young adults of both sexes. During the experiment the subject inhaled two gas mixtures alternately for 5, 10, or 15 min, one of them corresponding in composition to ordinary air, the other with a modified oxygen or carbon dioxide concentration. Guided by his own sensations, the subject could then select either of the offered mixtures. He justified his choice in his own words.

The subject inhaled through a mask connected to an improved spirograph [1]. The parameters of respiration and oxygen saturation of the arterial blood were recorded continuously.

Some experiments were carried out with free respiration: the spontaneous rate and depth of the subject's respiration were not restricted. In other experiments the subject was assigned a fixed pattern of respiration. The sliding contacts of the spirograph automatically switched on signals to the control panels of the subject and experimenter. As a first step, the subject's intrinsic rate and volume of respiration were determined. In later experiments an electrical metronome was tuned to the same rhythm, and the spirograph contacts were set as follows: when the subject had inhaled 90% of his mean respiratory volume, a white lamp lit up on the control panel, and when 110% of this volume was reached, a blue light lit up. In accordance with the command, the subject had to start the next inspiration at each beat of the metronome, and it continued until the white light lit up, and the object was to prevent the appearance of a blue light. The subjects quickly became accustomed to this steady pattern of respiration.

EXPERIMENTAL RESULTS

The increase in ventilation and decrease in oxygenation of the blood during free inhalation of hypoxic mixtures are illustrated in Fig. 1 (A). With a fixed pattern of respiration and inhalation of the same mixtures (B), the ventilatory response was absent. However, the oxygen saturation of the blood fell by almost the same amount as during free respiration. The experiments showed that this paradoxical fact may be explained by a decreased oxygen utilization during respiration under fixed conditions compared with analogous experiments in which respiration was unrestricted. Probably the cause of the relatively low gas ex-

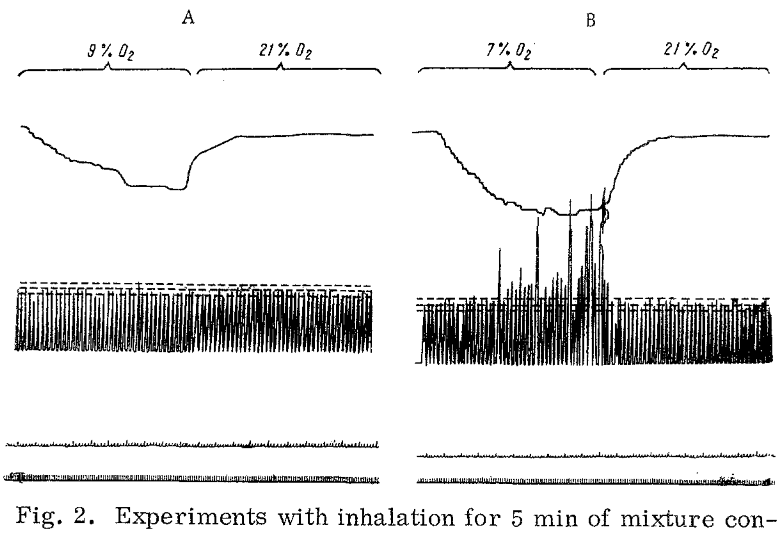

Fig. 2. Experiments with inhalation for 5 min of mixture containing 9% (A) and 7% (B) oxygen with a fixed pattern of respiration. From top to bottom: oxygen saturation of blood, spirogram, time marker 5 sec. Broken lines indicate respiratory volume specified for subject: top line-maximal, middle-normal, bottom-minimal. When inhaling mixture with 9% O_2, subject maintains this volume, when inhaling mixture with 7% O_2, starting from 3 min, disturbances occur—considerable deepening of respiration ceasing after switching over to air.

TABLE 1. Responses of Inhalation of Mixture Containing 7% Oxygen in Subjects Compared with Their Ability to Maintain an Assigned Pattern of Respiration in this Mixture

Group of subjects	No. of subjects	During free respiration				During fixed pattern of respiration	
		pulmonary ventilation (in liters/min)		blood oxygen saturation (in %)		blood oxygen saturation (in %)	
		initial	change during respiration of mixture (± t)	initial	change during respiration of mixture (± t)	initial	change during respiration of mixture (± t)
Maintaining assigned pattern	4	7.2	+ 1.2 ± 0.2	94.0	−16.7 ± 2.5	94.0	−17.9 ± 4.6
Not maintaining assigned pattern	8	6.7	+ 3.5 ± 0.6	94.0	− 27.0 ± 2.7	94.0	−27.7 ± 2.9

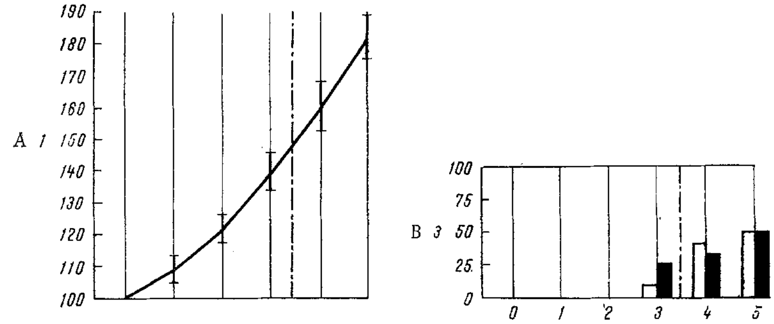

Fig. 3. Response of subject to hypercapnic mixtures during free (A) and fixed (B) patterns of respiration. Unshaded columns: cases when assigned respiration rate was exceeded; black columns: cases when assigned respiratory volume was exceeded. Abscissa: percentage of CO_2 in inspired mixtures. Remainder of legend as in Fig. 1.

change under these conditions was the absence of increased work of the respiratory muscles and the presence of conditioned-reflex connections between the level of metabolism and respiration, in that order of importance [4].

All subjects easily maintained a fixed level of ventilation while inhaling mixtures containing 21, 28, or 15% oxygen. Inhalation of 12 and 9% mixtures sometimes caused a disturbance of the assigned pattern, but only in some subjects and, in particular, in experiments when the mixtures were inhaled for 10-15 min at a time. During inhalation of a mixture with 7% oxygen, most subjects were unable to maintain the fixed pattern: after 3-5 min they began to show an involuntary deepening of respiration, although as a rule they maintained the assigned rhythm (Fig. 2). Some subjects, however, were able to inhibit their ventilatory response completely for 5 min, even when inhaling such a strongly hypoxic mixture.

The two groups of subjects, generally speaking, responded differently to hypoxia (Table 1). In the subjects who maintained a fixed pattern of respiration while inhaling a mixture containing 7% oxygen, during free respiration a weak ventilatory response was observed, and a smaller decrease in blood oxygenation was observed both during free respiration and during inhalation of hypoxic mixtures with a fixed pattern of respiration compared with subjects who failed to maintain the assigned respiration pattern. These differences were significant ($P < 0.05$). In some subjects, inhalation of mixtures poor in oxygen evidently produces an immediate and considerable hypoxemia and a marked ventilatory response, which they cannot inhibit voluntarily. In other subjects, however, inhalation of hypoxic mixtures is accompanied, as our calculations showed, by a decrease in oxygen utilization in the body, thus enabling the blood oxygenation to be maintained at a relatively high level while the partial pressure of oxygen in the surrounding medium falls, at least temporarily. The ventilatory response of such subjects, however, is weak and can easily be inhibited.

TABLE 2. Responses to Free Inhalation of Mixture Containing 5% CO_2 in Subjects Compared with Their Ability to Maintain an Assigned Pattern of Respiration in this Mixture

Group of subjects	No. of subjects	Pulmonary ventilation (in liters/min	
		initial	change during respiration of mixture (± t)
Maintaining assigned pattern	6	7.4	+ 4.1 ± 0.7
Not maintaining assigned pattern	6	7.4	+ 8.1 ± 0.9

Maintenance of a fixed pattern of respiration requires considerable effort, even with moderate hypoxia. This was evidently the factor determining the difference between responses of choice of mixtures: whereas during free respiration most subjects rejected (preferring air) mixtures in which the oxygen concentration was 10.5% or lower, during fixed respiration they rejected mixtures containing 15% oxygen (inhalation for periods of 15 min). Negative responses to these mixtures were expressed by the subjects' comments: "difficult to breathe" or "cannot get enough air."

Ventilatory responses of the subject to hypercapnic mixtures (A) and his ability to breathe such mixtures in a fixed pattern (B) for 5 min can be compared in Fig. 3. Disturbances of this fixed pattern were observed during inhalation of a mixture containing 3% CO_2, and when breathing a 5% mixture, half the total number of subjects were unable to prevent an increase in the frequency and depth of respiration.

The ventilatory response of those subjects who were able to suppress the increase in minute volume of respiration during inhalation of a hypercapnic mixture was only half the amplitude during free inhalation of this mixture compared with that of subjects whose fixed pattern of respiration was disturbed. In this case also, the subject's well-developed respiratory response was more difficult to inhibit.

In one of the series of experiments the respiration pattern was established at a modified, higher level. Initially, in the control experiment, the subject was instructed to breathe freely a mixture containing 3% CO_2 and 21% O_2 in nitrogen, and the frequency and depth of his respiration was recorded. The subject was expected to maintain the same pattern of respiration in the subsequent experiments.

During fixed hyperventilation of this type, the subjects were able to breathe a mixture containing 3% CO_2 without disturbance. However, it is interesting to note that most subjects, under these circumstances, preferred this mixture to "pure" air. Probably under these experimental conditions the subject actively avoided the hypocapnia which developed during hyperventilation with air, but which was abolished by an excess of CO_2. In this case the link between chemical and reflex mechanisms of regulation of respiration could play an important role. There is evidence that, because of the Hering–Breuer reflex, stretching of the lungs reduces the sensitivity of the respiratory center to carbonic acid [7]. An increase in the depth of respiration, as a result of this inhibitory effect from the mechanoreceptors of the lung, thus reduces the "conscious perception of the chemical stimulus" and enables the subject to maintain an assigned respiratory volume during inhalation of a mixture with higher concentrations of CO_2 [9].

In the same way, when a subject during fixed hyperventilation was offered hypoxic mixtures, the ability to maintain an assigned respiration pattern when the respiratory medium contained a lower oxygen concentration was demonstrated. The subjects inhaled hypoxic mixtures in preference, however, to ordinary air.

In response to a verbal command, man is thus capable of maintaining an assigned pattern (rate and depth) of his respiration if the oxygen and carbon dioxide concentrations in the respiratory medium lie between certain limits. These limits may differ depending on inequality of the respiratory response of individual subjects to hypoxic and hypercapnic stimuli. With a change in the assigned level of ventilation, the range of changes in composition of the respiratory medium within which the subject can maintain this level changes correspondingly. Under these conditions the sensations evoked by inhalation of the difference gas mixtures and reflected by the subject's spoken comments are also changed.

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