Mechanisms Compensating for Altered Resistance to Respiration During Muscular Exercise in Man

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Alterations in respiratory parameters following the substitution of a helium-oxygen ($He-O_2$) or sulfur hexafluoride-oxygen (SF_6-O_2) mixture for air were analyzed during the first 10 respiratory cycles in human volunteers exposed to either of these mixtures for 3 min at rest and during forced respiration. Both at rest and during moderate physical exercise neither the volume of pulmonary ventilation nor the partial carbon dioxide pressure differed significantly in the subjects breathing air, $He-O_2$, or SF_6-O_2. When the $He-O_2$ mixture was substituted for air, the forces developed by the inspiratory muscles, the work of breathing, the activity of the parasternal intercostal muscles, and the central inspiratory activity were all reduced, whereas substitution of the SF_6-O_2 mixture for air led to significant increases in these four parameters. It is concluded that compensatory responses of the respiratory system to altered density of the gaseous medium develop on the basis of the afferent impulse traffic from mechanoreceptors of the lungs and respiratory muscles and also on account of segmental reflexes and intrinsic properties of the muscle fibers themselves.

Key Words: *regulation of respiration; resistance to respiration; helium-oxygen mixture; sulfur hexafluoride-oxygen mixture; muscular work*

An increase in aerodynamic resistance to the gas flow in the airways (flow-resistive load) elicits adaptive changes in the functioning of respiration-regulating mechanisms which act to compensate for the additional load on the respiratory system. The volume of alveolar ventilation matching the metabolic rate is maintained through increased activity of the respiratory musculature and energetic optimization of the breathing pattern [1,8,15]. The compensatory reactions involve a number of mechanisms that actuate different levels of regulation, ranging from intrinsic properties of respiratory muscles to cortical influences [7,9].

In this study an attempt is made, based on a comprehensive assessment of each respiratory cycle (breath-to-breath), to analyze the mechanisms compensating for the increased or decreased internal resistance to the gas flow in the airways caused by inhalation of gaseous mixtures of different densities at rest and during moderate muscular exercise.

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MATERIALS AND METHODS

The subjects were 10 healthy men aged 22-24 years. They performed muscular work of constant power (equal to 50% of its maximal tolerable value for each subject) on a bicycle ergometer of the Monark type.

With the subjects in the resting state or exercising on the ergometer, a helium-oxygen ($He-O_2$) or sulfur hexafluoride-oxygen (SF_6-O_2) normoxic mixture was abruptly substituted for the air they were breathing through a mask. The density of SF_6-O_2 was 4.2 times higher than that of air,

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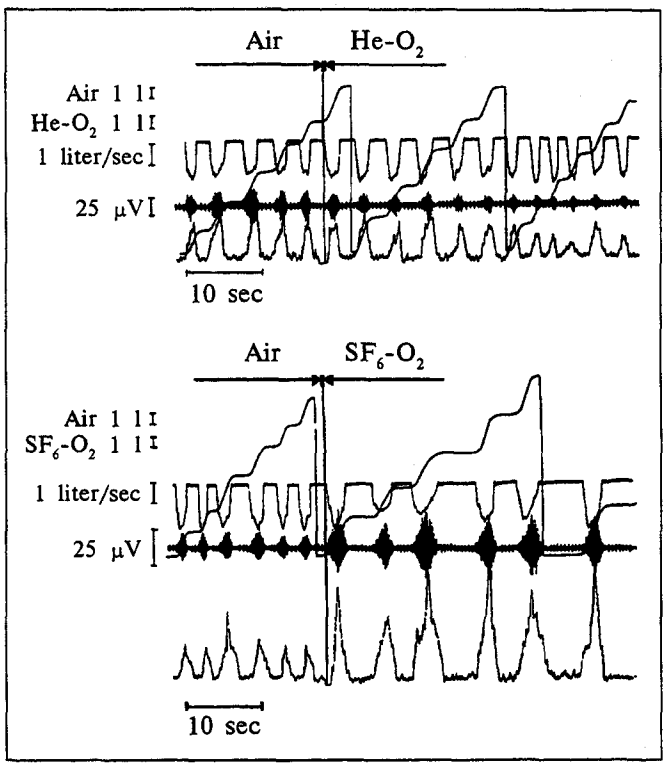

Fig. 1. Electrical activity of parasternal intercostal muscles, pneumotachogram, and respiratory volume before and after $He-O_2$ or SF_6-O_2 were substituted for air in a subject performing moderate muscular work. Top down: pneumotachogram, electromyogram, and biopotential envelope; the rising "steps" indicate respiratory volume. The vertical lines mark the instants when $He-O_2$ and SF_6-O_2 were substituted for air.

whereas the $He-O_2$ had a density 2.9 times lower than air. Each subject inhaled $He-O_2$ or SF_6-O_2 for 3 min.

Respiratory (tidal) volume, respiratory frequency, minute ventilation, and peak velocity of the inspiratory flow were calculated using pneumotachograms. Partial CO_2 pressure in the alveolar gas (Pco_2) was estimated with a capnograph from the composition of the final portion of exhaled air. Inspiratory pressure differentials inside the mask were used as a measure of the total effort developed by inspiratory muscles. The inspiratory work of breathing was calculated, and the electrical activity of the parasternal intercostal muscle in the second intercostal space was continuously recorded (under ordinary conditions, this muscle exhibits extremely high inspiratory activity). The initial respiratory activity was estimated by the maximal velocity (first derivative) of inspiratory pressure rise at the beginning of inspiration (dP/dt_I) [6].

RESULTS

As shown in Tables 1 and 2, the abrupt substitution of $He-O_2$ or SF_6-O_2 for air did not cause statistically significant changes in the minute ventilation, respiratory volume, respiratory frequency, or Pco_2 in the resting subjects. The peak inspiratory flow velocity ($V_{I_{max}}$) significantly increased during $He-O_2$ breathing, but fell during SF_6-O_2 breathing to the control values recorded once the subjects resumed air breathing. In the course of muscular work, the minute ventilation and Pco_2 both remained at a constant level when the subjects were breathing air, $He-O_2$, or SF_6-O_2, but the constancy of minute ventilation was maintained because of the significantly increased respiratory frequency at a lowered respiratory volume when the "light" $He-O_2$ mixture was inhaled and, conversely, because of the reduced respiratory frequency at an elevated respiratory volume during the inhalation of the "heavy" SF_6-O_2 mixture (Fig. 1). Variations in the peak

TABLE 1. Effect of $He-O_2$ Inhalation on Respiratory Parameters in the Subjects at Rest and during Constant Moderate Muscular Work

Parameter	Resting state			Work		
	air	$He-O_2$	air	air	$He-O_2$	air
V_E, liters/min	8.89±0.54	9.12±0.55	8.75±0.41	33.12±2.26	34.52±2.67	33.35±1.90
V_T, liters	0.86±0.18	0.90±0.18	0.82±0.15	2.03±0.18	1.90±0.17*	2.03±0.13
f, breaths/min	12.70±1.41	12.50±1.39	12.40±1.31	17.20±1.38	19.11±1.62**	17.70±1.78
$V_{I_{max}}$, liters/sec	0.42±0.02	0.57±0.04**	0.40±0.03	1.56±0.10	1.88±0.13**	1.61±0.09
Pco_2, mm Hg	32.14±1.26	33.53±1.20	31.01±1.00	44.76±1.06	44.93±1.04	44.51±1.17
P_{ml}, cm H_2O	0.70±0.05	0.46±0.07**	0.65±0.07	1.74±0.16	1.03±0.07**	1.92±0.17
W_I, kgm/min	0.061±0.006	0.043±0.007**	0.058±0.007	0.601±0.085	0.369±0.049**	0.692±0.093
dP/dt_I, mm H_2O/sec	32.40±3.17	23.30±2.88**	36.30±3.37	129.10±12.88	91.40±8.23**	133.00±16.38

Note. Here and in Table 2: V_E = minute ventilation; V_T = respiratory (tidal) volume; f = respiratory frequency; $V_{I_{max}}$ = peak respiratory flow velocity; P_{ml} = pressure differentials inside the mask on inspiration; W_I = inspiratory work of breathing. *$p<0.05$, **$p<0.01$ in comparison with air breathing.

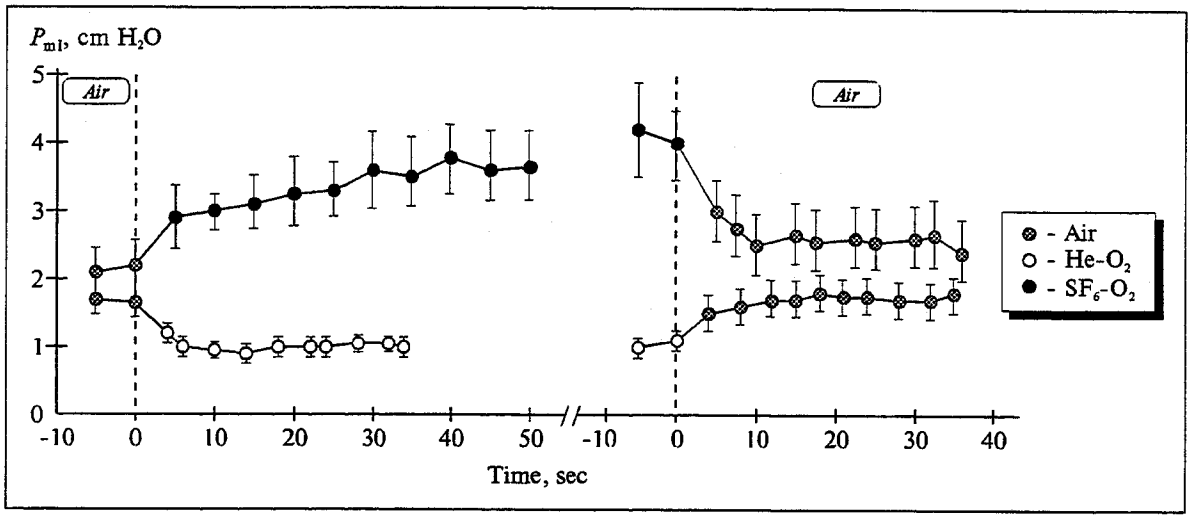

Fig. 2. Temporal variations in inspiratory pressure inside the mask (P_{ml}) after substitution of $He-O_2$ or SF_6-O_2 for air and vice versa during the first 10 respiratory cycles in subjects performing constant moderate muscular work. The vertical dashed lines mark the instants of the substitutions.

inspiratory flow velocity were much larger than in the resting state (Fig. 1).

The greatest changes occurred in the mechanics of breathing (Tables 1 and 2). In the resting subjects, the substitution of $He-O_2$ for air led to an abrupt fall in inspiratory pressure differentials inside the mask, whereas the substitution of SF_6-O_2 for air resulted in their rise. During exercise, under conditions of working hyperpnea, the changes in this parameter were similar, but more strongly marked. It is noteworthy that both at rest and especially during exercise, all changes that were recorded occurred beginning with the first few "loaded" or "unloaded" respiratory cycles (Fig. 2). Temporal variations in the inspiratory work of breathing were similar to those in the intra-mask pressure.

The peak of the envelope curve describing variations in biopotentials of the parasternal intercostal muscle during exercise dropped sharply (by 30% on average) when the subjects breathed $He-O_2$, rose nearly 2-fold when they breathed SF_6-O_2, and regained its control (initial) value as they resumed breathing air (Fig. 1).

Breathing the $He-O_2$ mixture appreciably reduced the central inspiratory activity both at rest and during muscular work. The transfer to SF_6-O_2 breathing was followed by significant increases in dP/dt_I values (Tables 1 and 2). The changes in dP/dt_I were rapid at rest and even more so during forced breathing (Fig. 3).

Since the minute ventilation and Pco_2 in the resting and exercising subjecting breathing air, $He-O_2$, or SF_6-O_2 were maintained at constant levels,

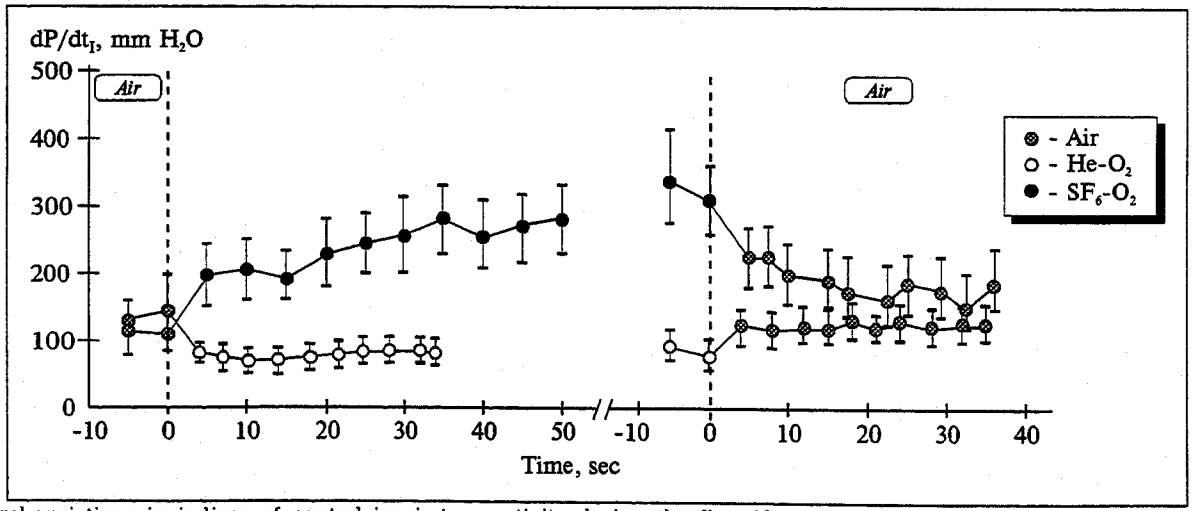

Fig. 3. Temporal variations in indices of central inspiratory activity during the first 10 respiratory cycles after substitution of $He-O_2$ or SF_6-O_2 for air and vice versa in subjects performing constant moderate muscular work. The vertical dashed lines mark the instants of the substitutions.

TABLE 2. Effect of SF_6-O_2 Inhalation on Respiratory Parameters in the Subjects at Rest and during Constant Moderate Muscular Work

Parameter	Resting state			Work		
	air	SF_6-O_2	air	air	SF_6-O_2	air
V_E, liters/min	9.01±0.69	8.95±0.55	12.63±1.86	31.97±2.45	33.55±2.24	36.42±2.51
V_T, liters	0.86±0.17	0.94±0.15	0.92±0.23	2.00±0.20	2.58±0.28**	2.27±0.26
f, breaths/min	12.25±1.51	11.30±1.65	12.25±1.73	17.10±1.52	14.40±1.45**	18.10±1.91
V_{Imax}, liters/sec	0.44±0.02	0.34±0.02**	0.64±0.09	1.52±0.10	1.46±0.12*	1.86±0.14
Pco_2, mm Hg	33.25±0.73	33.40±0.98	33.15±1.07	45.70±0.71	47.43±1.14	44.03±1.27
P_{mI}, cm H_2O	0.74±0.05	1.05±0.03**	0.92±0.06	1.87±0.20	3.84±0.42**	2.42±0.33
W_I, kgm/min	0.066±0.008	0.096±0.007**	0.121±0.027	0.624±0.099	1.339±0.179**	0.941±0.169
dP/dt_I, mm H_2O/sec	32.70±3.38	57.80±8.19**	37.90±3.79	117.80±13.24	289.30±33.70**	162.80±13.55

it appears that the compensation for loading or unloading of the respiratory system is mediated by neurogenic regulatory mechanisms that come into play rather than by chemical agents. The maintenance of ventilation at a level high enough to meet the requirements of muscular work during the inhalation of a gaseous mixture of decreased or increased density as compared to normal air is made possible both by the energetically optimal reorganization of the breathing pattern and by alterations in the exertions of the inspiratory muscles and in the central inspiratory activity. The observed rapid changes in the volume and temporal parameters of respiration following the replacement of air by $He-O_2$ or SF_6-O_2 during muscular exercise were apparently associated with the functioning of the pulmonary afferent system. Inhaling the denser gaseous mixture (SF_6-O_2) resulted in a diminished inspiratory flow rate and thus in a lesser stimulation of the receptors sensitive to the dynamic component of lung distension and in a weakening of their inhibitory influence on the central inspiratory activity; as a consequence, the inspirations became longer and of greater volume. Conversely, inhaling the less dense gaseous mixture ($He-O_2$), which reduced the nonelastic resistance to respiration, led to a rise in the inspiratory flow rate.

When the lungs rapidly fill with a $He-O_2$ mixture during forced breathing, the distension receptors are probably additionally activated, promoting an early interruption of the central inspiratory activity and, consequently, a shortening of the inspiratory phase. Experiments with anesthetized animals demonstrated that the responses to loading or unloading of respiration involve the vagal reverse phase [2,3].

The most important role in compensating for altered resistance to the gas flow is played by the afferent system of the respiratory muscles and, in particular, the intercostal muscles [4,5,11]. We found that the inspiratory efforts, electrical activity of intercostal muscles, and the work of breathing all increased or decreased after the first few respiratory cycles once the subjects started to breathe SF_6-O_2 or $He-O_2$, respectively, instead of air. Under these conditions, a reflex of "load compensation" kicks in, whereby the impulse traffic from the endings of muscle spindles is enhanced as a result of the mismatching of extrafusal and intrafusal fibers due to insufficient shortening of the inspiratory muscles in the face of increased resistance to the inspiratory flow. This afferent impulse traffic ensures both the additional activation of appropriate α-motoneurons in the spinal cord and information transfer to bulbar structures [5-10]. As a consequence, the central inspiratory activity rises or falls depending on the density of the inhaled gaseous mixture, the ultimate result being enhanced or diminished force with which the respiratory muscles contract [11,12].

Also contributing to the compensatory responses to the loading and unloading of respiration are those properties of the inspiratory muscles themselves which determine the dependence of their contraction force on the rate of their shortening and on their initial length [13,14].

The results of this study lead to the following conclusions. The afferent impulse traffic from distension receptors of the lungs is implicated in shaping the breathing pattern in subjects inhaling a gaseous mixture of increased or decreased density for a short time while performing muscular work. Afferent information from proprioceptors of respiratory muscles is involved in the compensatory increases that are observed. Efforts of the respiratory musculature are reduced both by mechanisms of the segmental level (and also because of

the intrinsic properties of muscle fibers) and as a result of afferent information reaching respiratory structures of the medulla oblongata. The upshot is altered central inspiratory activity.

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