Cardiorespiratory and performance changes in graded hypoxia simulated with gas mixtures

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Twenty-six subjects were exposed to equivalent altitudes of 6000 ft, 8000 ft and 12,500 ft using gas mixtures with oxygen concentrations of 18.4%, 17.1% and 14.1%, respectively. The subjects were monitored for various physiological parameters like heart rate, blood pressure, respiratory rate, ventilation, end tidal CO_2, transcutaneous oxygen and CO_2 tensions. Performance was assessed using a validated psychomotor task. The physiological changes were similar to the results reported in simulation studies using altitude simulator. The potential use of gas mixtures as a research tool, especially for field studies, is discussed.

Keywords: Hypoxia; Gas mixtures; Psychomotor performance.

Ever since the ascent of man in a balloon, hypoxia has been recognized as a major flight hazard. Tactical combat flying today is restricted to altitudes below 15,000 ft and as such aircrew are exposed only to hypoxia of lower altitudes (<10,000 ft) because of the use of oxygen systems and cabin pressurization. Recently, research on hypoxia has concentrated on performance decrement at these lower altitudes, as any reduction in performance may make all the difference for a successful mission outcome [1–3].

Amongst the various methods that have been developed for the simulation of hypoxia, the low-pressure chamber is the most accurate in simulating the effects of high altitudes [1, 4]. However, the installation and maintenance of a low-pressure chamber is expensive, and also it cannot be used with a combination of stressess, e.g. vibration, heat, etc. The use of low-O_2 (< 21%) breathing gas mixture is an alternative and effective method for the study of hypoxia in combination with other stresses.

This study used low-O_2 breathing gas mixture for ground-based simulation of hypoxia and reports the effects of three different levels of acute to moderate hypoxia on psychomotor performance and other cardiorespiratory variables.

Material and methods

Altitudes of 6000, 8000 and 12,500 ft were simulated by reducing the FiO_2 to 0.184, 0.171 and 0.141, respectively. Twenty-six healthy adult male volunteers with a mean age of 28.9 ± 4.2 yr were divided into three groups, eight each for 8000 and 12,500 ft and ten for 6000 ft.

Equipment assembly. The gas mixtures with the reduced oxygen concentrations were prepared commercially. These gas mixtures were stored in 7 m^3 cylinders at a pressure of 125 kg/cm^2. A combined contents gauge and pressure reducer mounted on top of the cylinder reduced the pressure to between 6 and 30 kg/cm^2, the working pressure of the regulator. A high-pressure tubing connected the cylinder to an Mk 17E pressure demand diluter regulator. The mixture of gases was delivered to the subject by means of an ABEU MK I/II (based on the RAF P/Q type) aviators oronasal mask. The expiratory snout of the mask was

modified by means of a metal tube to fit an Ohmeda volumeter.

Experimental protocol. The subjects were explained the experimental protocol and familiarized with the psychomotor performance task. Each subject then undertook at least 5 to 6 trials of the task. This ensured that the subject had learned the task sufficiently well prior to the conduct of the experiment. He was then connected to the system and the regulator was put at 'OFF', thus ensuring that he was breathing ambient air only. Physiological parameters were recorded at the 10th and 20th min of this phase and included heart rate (HR), blood pressure (BP), minute expiratory volume (VE) (recorded on an Ohmeda volumeter), respiratory rate (RR), end tidal CO_2 tension ($ETpCO_2$) ($ETpCO_2$ and RR were recorded on an Eliza Duo Gas Analyser, M/s Engstrom, Sweden) and transcutaneous O_2 and CO_2 tensions ($TcPO_2$ and $TcPCO_2$) (recorded on TINA transcutaneous oximeter TCM 3, manufactured by M/s radiometer, Denmark). Psychomotor performance was tested at the 10th and 20th min of the pre-hypoxia phase prior to recording of the physiological parameters. The test used, which was developed and validated at this Institute [5, 6], was a computerized version of the Red and Black table. This test combines visual vigilance, speed of perception of complex detail, short-

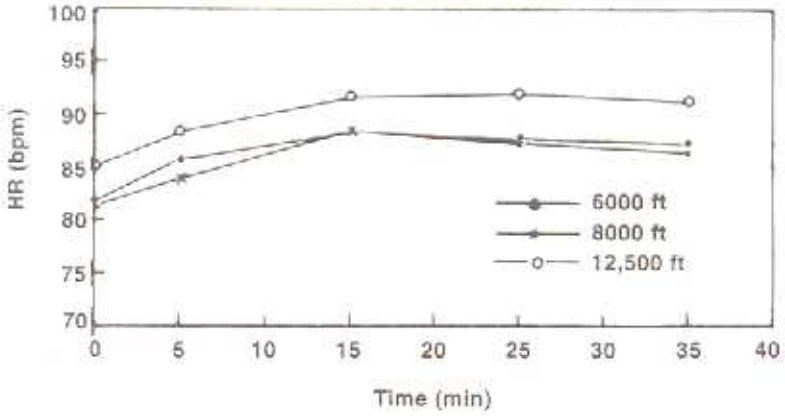
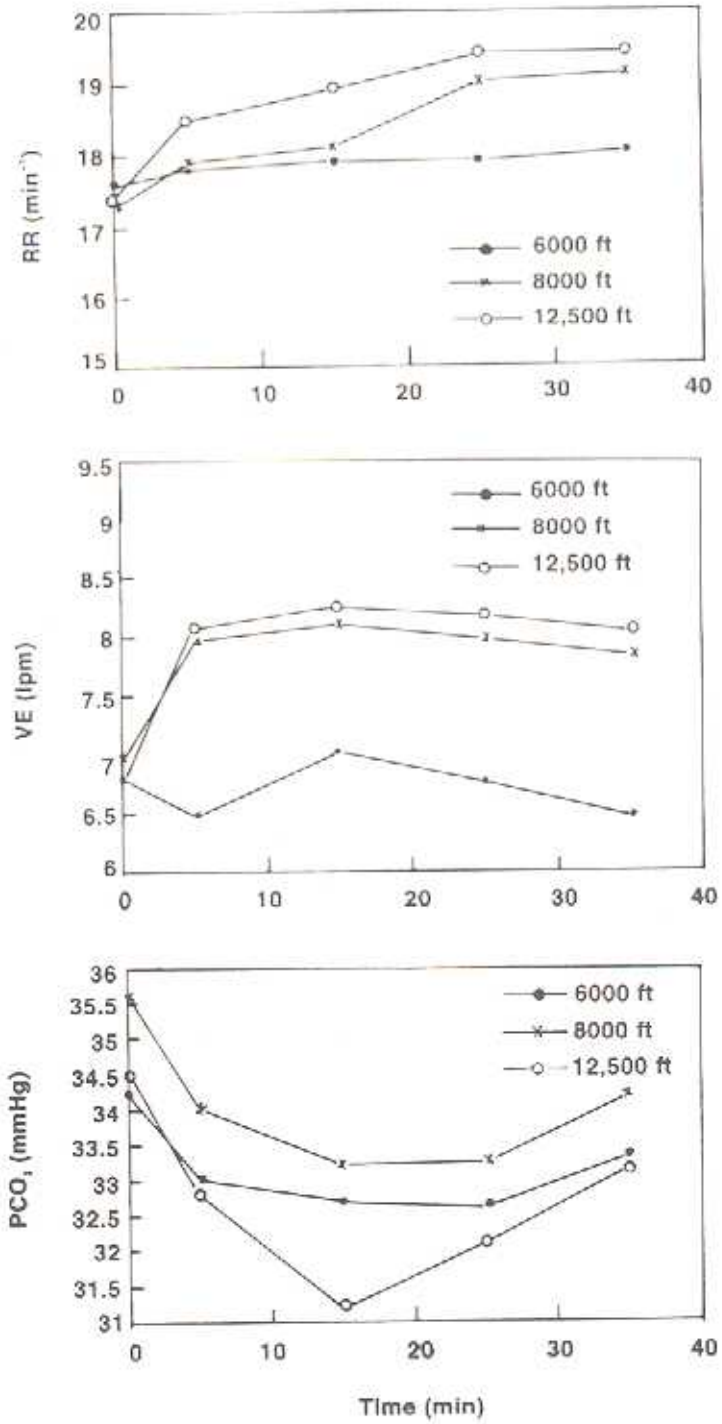


Figure 1. Heart rate response

Table I. Subjective symptoms at various altitudes

Subjective symptoms	No. of subjects at various heights (ft)		
	6000 ($n = 10$)	8000 ($n = 8$)	12,500* ($n = 8$)
Headache	–	1	1
Burning sensation in nose	1	1	2
Dizziness	2	1	3
Uneasiness	1	–	1
Inability to concentrate	–	–	2
Air hunger	–	–	2*

*At 12,500 ft some subjects had more than one symptoms



Figures 2, 3, 4. Respiratory rate response. Minute ventilation response. ETpCO2 response

term memory and choice reaction time. The test was performed on a PC AT 386SX. On completion of the recordings of the prehypoxia phase, the regulator was set to 100% and switched on, ensuring that the subject breathed only the gas mixture. The physiological as well as psychomotor performance was recorded at the 05th, 15th, 25th and 35th min of the hypoxia phase. On completion of the last set of recordings, the regulator was switched off and recovery from hypoxia was monitored for 20 min.

Results

Subjective symptoms were noticed at all altitudes and a break-up of these symptoms is given in Table 1. The severity and the number of subjects who complained of symptoms increased with the increasing altitude.

HR showed an increase till the 25th min, after which it tended to decrease. The increase in HR was proportionate to the level of hypoxia induced (Figure 1). The magnitudes of the increase in HR of 6.8 bpm at 1829 m, 7.2 bpm at 2438 m and 6.8 bpm at 3810 m were all statistically significant. The mean values of arterial BP did not show any appreciable change during exposure from the pre-exposure values at all the three levels of hypoxia simulated. The mean values of RR did not show any significant changes in response to the three simulated levels of hypoxia (Figure 2). At all three simulated-altitudes an increased till the 20th min of exposure and thereafter a gradual falls towards the pre-exposure level (Figure 3). The increases in VE of 1.2 lpm and 1.89 lpm at 1829 m and 8000 ft were not significant; however, the increase in VE of 1.47 lpm at 3810 m was significant. Post-exposure VE tended to be higher than the baseline values, but this was not significant. The response of tidal volume (VT) to hypoxia was similar to that exhibited by VE. There was no appreciable change from baseline values at 1829 m and 2438 m; however, an increase of 119 ml at 3810 m was significant.

The response of $ETpCO_2$ to hypoxia was similar at all three simulated altitudes (Figure 4). There was a significant fall till about the 15th to 25th min of exposure, followed by a gradual rise towards baseline values. However, even at the end of the hypoxia phase the decrease from baseline values was still significant. Post-exposure $ETpCO_2$ recovered to baseline levels quickly.

The $TcPO_2$ showed highly significant decreases at all three simulated altitudes proportionate to the degree of hypoxia induced and recovered to pre-exposure values during the post-exposure phase. The values of $TcPO_2$ observed at the three altitudes are shown in Figure 5.

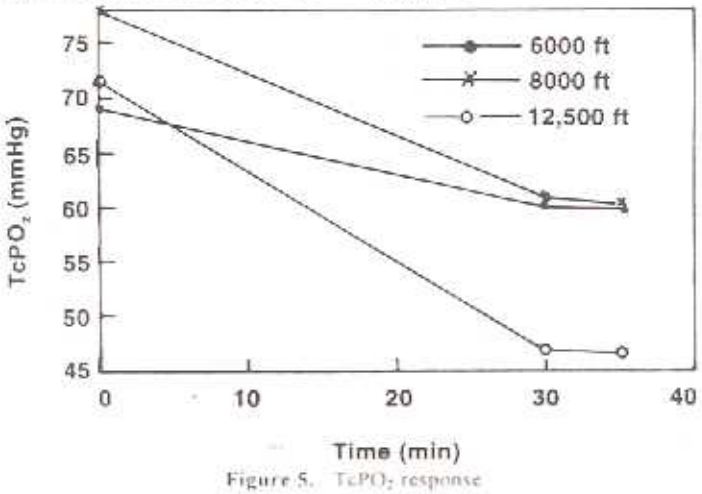


Figure 5. $TcPO_2$ response

Table 2. Psychomotor performance scores at various altitudes

Altitude (ft)	Psychomotor test score (mean ± SD)		
	Pre-exposure	Hypoxia	*p* value
6000 ($n = 10$)	13.36 ± 3.46	13.16 ± 4.35	NS
8000 ($n = 8$)	15.26 ± 4.05	15.20 ± 4.52	NS
12,500 ($n = 8$)	13.60 ± 3.65	10.28 ± 3.59	$p < 0.01$

NS Not significant

There were decrements in psychomotor performance at all three altitudes, with the decrement being significant only at 12,500 ft. The mean scores achieved in the psychomotor performance task tested at the 25th minute of exposure to hypoxia at the three simulated altitudes are shown in Table 2.

Discussion

Hypoxia causes a fall in PAO_2 and consequently a decrease in PaO_2. At sea level the PAO_2 is about 96–98 mmHg and the SaO_2 is about 97%. With increasing altitude, breathing air consequent to the fall in ambient pressure, the PAO_2 decreases to 72 mmHg at 6000 ft, 63 mmHg at 8000 ft and 46 mmHg at 12,500 ft [2, 3]. This decrease in PAO_2 was produced by lowering the FiO_2 using a mixture of gases. Following exposure to such a gas mixture, physiological equilibration takes place in about 10 min [7]. The symptoms of hypoxia and those due to the compensatory mechanisms appear subsequent to this time frame. However, there are large inter- and intra-individual differences on exposure to altitude [1, 3, 4, 8].

The fall in PaO_2 in hypoxia initiates reflex respiratory and circulatory compensatory responses within the body, mainly mediated through the peripheral chemoreceptors, which are most sensitive to hypoxic insults [1, 9]. The integrated effect of these reflex responses is an increase in pulmonary ventilation, increase in HR and a beneficial redistribution of the cardiac output [9, 10]. However, the compensation is not complete and usually some deterioration in performance may occur above 10,000 ft altitude [2, 3, 11].

The development of subjective symptoms is not an indicator of the severity of hypoxia. Symptoms like dizziness and blurring of vision may be the manifestations of the compensatory response to hypoxia and the direct neurological effects of hypoxia on the CNS. However, most of these symptoms tend to settle down towards the end of the hypoxic exposure. This indicates the onset and establishment of the various compensatory mechanisms as a result of which the symptomatology tends to decrease [2–4].

It is well known that an acute exposure to hypoxia causes an increase in the HR and cardiac output [1, 4, 10]. The increase in HR has been shown to begin from an altitude as low as 4000 ft [2, 3]. The increase in HR has been attributed to two factors; firstly, there is a response spillover to the vasomotor centre from the respiratory centre and, secondly, due to reflex chemoreceptor activity. The greater the hypoxic insult, the greater will be the stimulation of the chemoreceptors and the greater the increase in HR [9]. This is reflected in our study, where the increase in HR was found to be proportionate to the altitude simulated.

The arterial BP usually does not show any change on exposure to acute hypoxia [1, 3, 4, 10], and this again was corroborated in the present study.

The classical respiratory response to hypoxia is an increase in tidal volume with a corresponding increase in minute ventilation, mediated by the chemoreceptors [3, 4, 9]. However, large inter- and intra-individual differ-

ences are seen; thus, these changes may be seen at as low as 1219 m in a sensitive individual, while in others no change may be appreciable till about 3658 m [3, 5, 8]. Respiratory rate increase is seen classically at altitudes above 3658–4572 m [4, 9]. The increase in VE, in turn, causes a decrease in $PACO_2$ (manifested as a decrease in $ETpO_2$) and a consequent decrease in $PaCO_2$. The decrease in $PaCO_2$ tends to cause a decrease in VE and the hypoxic ventilatory drive now becomes predominant [4, 8]. These changes were closely paralleled in our study and showed a linear response to increasing altitude.

Transcutaneous oximetry is an indirect correlate of arterial oxygen saturation and serves as an objective criterion for the degree of hypoxia induced. However, its correlation with blood gas is only 0.79 in adults [12]. $TcPO_2$ tends to show lower values than the actual blood gas. The fall in $TcPO_2$ is due to the fall in PiO_2 and that of $TcPCO_2$ is due to the fall in $PaCO_2$ consequent to the hypoxia-induced hyperventilation. In this study both $TcPO_2$ and $TcPCO_2$ showed a significant fall from 1829 m onwards, with the degree of fall being proportionate to the degree of hypoxia induced.

Of primary concern in aviation is the possible decrement in performance on exposure to altitude. It is generally accepted that the effects of hypoxia upon cognitive functions become significant only above 3048 m [3, 11, 13, 14]. However, recent studies have shown that there may be a decrease in performance at altitudes as low as 1524 m [11, 15, 16]. Recent memory and complex choice reaction times are some of these affected at the earliest [11, 16]. The deterioration in performance is, however, again subject to marked inter- and intra-individual differences. In some subjects an exposure to hypoxia causes euphoria, probably due to the stimulation of ascending reticular activating system, which may lead to an improvement in the psychomotor performance [1, 3, 11].

In this study a complex number-sorting test which measures the speed of perception, shifting of attention, visual vigilance and immediate memory was used to measure psychomotor performance. The results obtained are consistent with those of other workers in that the decrement in performance was not significant at 1829 m and 2438 m. However, at 3810 m the decrement in performance was highly significant. These results can be explained by the fact that hypoxia of less than 3048 m is not sufficient to cause a significant decrement in performance, but at 3810 m cognitive functions are affected and hence a significant decrement in performance was noticed. Alternatively, the task may not have been sensitive enough to detect the minute changes in performance which have been shown to occur from 1524 m upwards.

Conclusion

This study has corroborated the use of low-oxygen breathing mixtures in the simulation of hypoxia. The changes in the various cardiorespiratory and performance parameters seen with graded hypoxia exposures in this study are similar to those reported on exposure to simulated altitudes in decompression chambers. The primary advantage of this simple method lies in that it can be used to simulate hypoxia either singly or in combination with other aviation stresses.

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