

# Hypoxia familiarisation training by the reduced oxygen breathing method

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EXPOSURE TO THE ATMOSPHERE AT ALTITUDE threatens aviators with decompression sickness, hypobaric hypoxia, and cold.<sup>1</sup> The resulting visual symptoms (eg, partial or complete blindness), cerebral symptoms (eg, partial paralysis of a limb), or degraded cognitive function can have catastrophic consequences.<sup>1</sup> Because of the possibility of decompression in aircraft flying at medium to high altitudes,<sup>2</sup> or failure of an oxygen mask or regulator,<sup>3</sup> training in the recognition of the early signs of cerebral or cognitive impairment due to hypobaric hypoxia is important.<sup>1-4</sup>

Cable has reported a significant number of in-flight hypoxia incidents in military aircraft and their causes, confirming the importance and effectiveness of hypoxia training.<sup>3</sup> The individual variability in susceptibility to hypobaric hypoxia is an argument for considering mandatory hypobaric chamber training of all active service pilots and aviation medical personnel.<sup>1-4</sup> At present, all active service pilots and medical graduates undergo mandatory training and pilots have familiarisation training every 2 years. Other aviation medical personnel are offered training which is not mandatory.

However, the risk of inducing decompression sickness in traditional chamber runs at a simulated altitude of 25 000 feet (7620 m) is sufficiently high (affecting 0.15%–0.44% of subjects in one large study)<sup>2</sup> to prompt consideration of safer alternatives. Moreover, a hypobaric chamber is not always available for all the groups who could benefit from hypoxia training. An alternative is the use of a reduced oxygen gas mixture to induce hypoxia at normal pressures. In 2001 Sausen et al reported that reduced oxygen breathing for inducing normobaric hypoxia in a group of 12 US Navy divers produced results comparable with hypobaric chamber training.<sup>4</sup> Here I describe the results of hypoxia training by reduced oxygen breathing for 476 subjects at Monash University, Victorian Air Ambulance Service, and ACT Ambulance Service.

## Methods

### Reduced oxygen gas mixture and delivery system

To create hypoxic conditions equivalent to an altitude of 25 000 feet (7620 m) one must reproduce the ambient partial pressure of oxygen (PO<sub>2</sub>) at that altitude (56 mmHg at the barometric pressure of 282 mmHg).<sup>5</sup> At that altitude, military aircraft oxygen demand regulators usually supply 62% oxygen and positive pressure to maintain 96%–98% oxygen saturation of arterial blood.<sup>5</sup>

The reduced oxygen gas mixture used in hypoxia training (supplied by British Oxygen Corporation [BOC]) was between 6%–7% oxygen (remainder nitrogen) and bracketed an ambient PO<sub>2</sub> of 56 mmHg. The gas mixture was held in new 100L

## Abstract

- ◆ **Background:** Hypoxia familiarisation training demonstrates and measures (1) cardiorespiratory adjustments in healthy volunteers to a simulated altitude of 25 000 ft (7620 m); (2) the spectrum of signs and symptoms accompanying hypoxia; (3) individual variability in susceptibility to hypoxia and oxygen paradox; and (4) time of useful consciousness. Trainees experience the insidious onset and obvious performance decrements resulting from hypoxia. Hypobaric chambers are traditionally used for this purpose, but carry a risk of inducing decompression sickness in trainees. An alternative is the use of low oxygen gas mixtures to simulate breathing conditions at high altitude.
- ◆ **Methods:** Subjects breathed a reduced oxygen gas mixture (6%–7% oxygen, balance nitrogen) and undertook repeated written tests of cognitive function until obvious impairments were observed. Blood oxygen saturation (SaO<sub>2</sub>), pulse rate, blood pressure, and ventilation were monitored throughout.
- ◆ **Results:** Cardiorespiratory physiological adjustments observed in 452 subjects included tachycardia (increase in heart rate ranging from 10–67 beats per minute), hyperventilation and cyanosis. Many subjects showed neuromuscular incoordination, tremor, twitching, illegible writing and poor reproduction of geometric figures. Simple arithmetical calculations and immediate and delayed recall were frequently impaired, usually when SaO<sub>2</sub> was between 45% and 60%. Perseveration of thought (expressed in writing) was common. Visual symptoms, dysaesthesia and headache were often described.
- ◆ **Conclusions:** Reduced oxygen breathing to simulate 25 000 ft altitude sessions is a safe, convenient and cost-effective way to train and familiarise aviators and medical and paramedical personnel with the effects of hypoxia.

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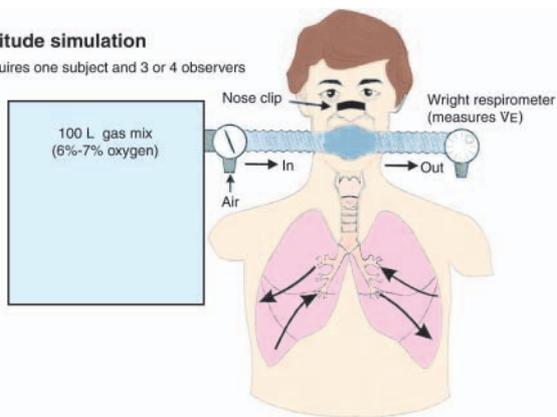
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## I: Reduced oxygen breathing apparatus

### Altitude simulation

Requires one subject and 3 or 4 observers



Schematic diagram of the breathing circuit used in hypoxia training. Corrugated plastic tubing is shown connecting the 2-way tap and gas bag to the inlet of the SCUBA mouthpiece, and also connecting the SCUBA mouthpiece outlet to room air via the Wright respirometer. The internal one-way valves inside the SCUBA mouthpiece are not shown.

flexible bulk milk-bags with a 2-way tap. These bags were filled from the cylinder of gas mixture supplied by BOC before connection to the subject. A corrugated hose connected the bag and tap to a SCUBA mouthpiece, with one way valves expiring to air (Box 1 and Box 2). Test subjects wore a nose clip, with continuous Propaq monitoring of oxygen saturation ( $\text{SaO}_2$ ), pulse rate (HR) and blood pressure (BP), and monitoring of ventilation frequency ( $f$ ) and expired volume (VE) via a Wright respirometer on the expiratory hose. Tidal volume (VT) was calculated from  $f$  and  $\text{VE}$  ( $\text{VE} = \text{VT} \cdot f$ ).

### Participants

The participants in these hypoxia familiarisation exercises were medical students, air ambulance trainees, and medical postgraduate students. All were consenting volunteers. An explanatory briefing preceded each training session. Possible medical reasons for non-participation in the hypoxic experience were discussed. It was emphasised to the groups that participation was voluntary, and that approval had been obtained from the relevant Monash University Ethics Committee. Trainees were then invited to sign a consent form or to remain in their groups as observers only.

### Procedure

Groups of 5 or 6 trainees were used. While one trainee underwent hypoxia training, the others performed the physiological and cognitive monitoring tasks. One experienced, medically qualified coordinator supervised two groups of trainees at a time.

For each trainee, a written “pencil and paper” cognitive function test (Box 3) lasting 90 seconds was administered at least once before exposure to reduced oxygen gas mixture, and then repeatedly during exposure. The hypoxic exposure was

stopped as soon as the subject had made two errors on the cognitive function test.

Physiological measurements commenced while subjects were breathing air before hypoxic exposure, and continued throughout the entire exposure and then for at least 2 minutes after they resumed breathing room air.

After recovery, each participant was asked to write down their subjective experience, with particular focus on symptoms, sensations or any other subjective observations they had made during and after the hypoxic exposure. Although no specific visual function or visual field tests were performed, A4 cards showing a variety of colours were displayed to the subjects before and during the hypoxic exposure, and they were asked after the study to recall their impressions of the colours.

## Results

Four hundred and seventy-six students and trainees were offered hypoxia training between 1989 and 2002 and signed the consent form. Of these, 24 declined to complete the procedure because of respiratory discomfort from the equipment and participated only as observers.

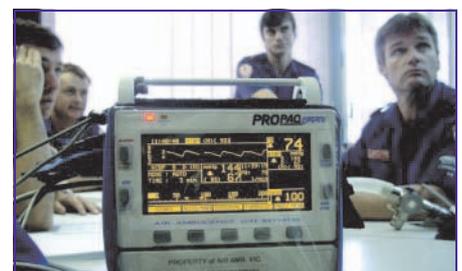
Physiological data obtained from the 452 subjects who completed hypoxia training are summarised in Box 4. For

## 2: Hypoxia familiarisation training

A. A subject using the reduced oxygen breathing apparatus. The other trainees (see B) are performing monitoring tasks. Note the gas mixture held in the gas bag, the two-way tap and connections to the mouthpiece, and the pencil and paper cognitive function test.



B. Propaq read-out of pulse rate and oxygen saturation.



### 3: Cognitive function tests used during reduced oxygen gas mix hypoxia familiarisation

#### Procedure:

- Instruct the subject to perform the cognitive function tests with a pencil and paper.
- After connecting the subject to the monitoring equipment and mouthpiece, but before commencing reduced oxygen breathing, perform baseline cognitive function tests. This familiarises the subject and recording observers with test and breathing equipment, and establishes baseline function.
- Repeat the tests during hypoxic exposure, beginning after 2 minutes of hypoxic exposure. Record the time at which each test is administered, in minutes and seconds, after commencing reduced oxygen breathing.
- When the first full sequence of tests has been administered, repeat the tests using the alternative re-test options to avoid practice effects.
- Halt the tests and reduced oxygen breathing after two cognitive errors or one error followed by incapacitation.

#### Tests:

**1. Simple computational problems:** addition, subtraction or multiplication.

**2. Serial 7 subtractions:** "Please subtract 7 sequentially from every answer, starting at 200. Do as many subtractions as you can in the 20 seconds allowed." Give an example, eg. From 100, it would be 93, 86, 79, etc. For re-tests, instruct the subject to start from a different number, eg. 105, or 110. This ensures that the task remains relatively novel and there is no direct learning. Errors may be numeric, but slowed processing or even thought block may be evident in this task.

HYPOXIA DEMONSTRATION SHEET	
LIST YOUR SYMPTOMS	TRY THESE PROBLEMS
1.	1. 1313 6792 3695 666
2.	2. -1212 +4981 X 5 -965
3.	3. SUBTRACT 7 FROM 100 :-
4.	4. DRAW A FIVE POINTED STAR
5.	4. WRITE YOUR NAME.

**3. Eye-hand coordination:** (a) "Please draw a five-pointed star using the pencil and sheet of paper provided." (b) "Please copy the figures from this sheet as quickly and exactly as you can." The figures include a 3-dimensional wire cube and 2 overlapping pentagons. Errors in lines at angles and intersections are scored to assess impairment of eye-hand coordination.

**4. Semantic memory and visual-motor coordination:** "Please complete the spoken phrase by writing it in full on the sheet of paper provided." Example: "The quick brown fox" — (jumped over the lazy dog).

**5. Recent memory:** (a) "Please memorise the 7 digit number which I will now say to you, and then write it on the sheet of paper." The tester should choose an unlikely or random order of numbers, not a recognisable sequence (eg, 7 2 9 1 4 6 8). If possible, repeat this test immediately before completing the hypoxic exposure. Errors often take the form of transposition of numbers or omission of one or more digits.

(b) "Please memorise this name and address exactly as I read it out to you, and write it down on the sheet of paper." Use a different name and address for different subjects. Example: James Bagel, 17 Wilson Road, South Esk.

**6. Graphic memory and coordination task:** "Please draw accurately 10 minutes to 7 on this clock face." (a blank circle with a central dot.) The subject must draw a short and long hand to correctly depict the stated time. A different time should be used for each repetition.

technical reasons, the Wright respirometer and Propaq were not available for all subjects, so statistical analyses were conducted on those who did have such monitoring. Because the hypoxic exposure was ended when one or more cognitive impairments were observed in addition to cyanosis, the duration of exposure is roughly equivalent to the time of useful consciousness (depending upon the definition used).

Box 5 sets out the subjective symptoms and observations made in writing by all subjects immediately after recovery. Box 6 summarises the incidence of observed impairments in pencil and paper cognitive function tests.

Oxygen paradox (ie, temporary increase in hypoxic symptoms on restoration of normal oxygenation) was noted in at least 6 subjects. Oxygen paradox may have been more common, but the protocol of the study is likely to have minimised its occurrence. At the end of the hypoxic exposure, subjects were returned to breathing room air. If, after 1–2 minutes, they had a persisting headache or felt unwell they were given 100% oxygen to breathe. Thus, in most subjects, the restoration of the alveolar PO<sub>2</sub> to normal was not as sudden as it would be if 100% oxygen had been administered immediately. Ernsting<sup>1,6</sup> suggests that oxygen paradox usually occurs in subjects who have become severely hypocapnic during the hypoxia, but in this study we did not measure end-tidal PCO<sub>2</sub>.

## Discussion

All the air ambulance trainees, medical students, and medical postgraduate students who participated in this altitude simulation study were healthy, consenting volunteers (similar to military personnel).

### Physiological cardiorespiratory adjustments (Box 4)

Because of the sigmoid shape of the oxygen-haemoglobin dissociation curve, the body is fairly well able to cope with the effect of reduced oxygen partial pressure for a short time. However, chemoreceptors, which are strategically located on the carotid and aortic arterial outputs monitoring the oxygen partial pressure, provide sensory signals which powerfully stimulate increased ventilation and cardiac output as the PaO<sub>2</sub> falls.

In this study, the cardiorespiratory physiological adjustments initiated by chemoreceptive afferent input are shown in Box 4. The falling SaO<sub>2</sub> is an indirect indicator of the reduced PaO<sub>2</sub>. Although individual variations are evident, universal cardiorespiratory physiological adjustments observed in 452 subjects (178 women, 274 men) included tachycardia (heart rate increase 9–65 bpm, mean increase 31 bpm), hyperventilation (increased VE, increased VT, increased f), and cyanosis.

Because the mean HR was 89 bpm while breathing air through the mouthpiece before hypoxic exposure, one may assume that there was both some anxiety and/or some increased ventilatory work. At the end of exposure to hypoxia the mean VE was 17.8 L/min, f was 14.6 and VT was 1.22 L. All subjects reported awareness of “increased breathing”, and 24 subjects terminated the exposure prematurely because of respiratory distress which they later ascribed to the resistance of the breathing equipment. All subjects exhibited increased minute ventilation volume, but some who showed a reduction in respiratory frequency (and a greater increase in tidal volume) described awareness of a “difficulty in breathing through the mouthpiece and system”. From this, one may assume that the non-volitional adjustments of ventilatory parameters in each subject were aimed at minimising the increased work of breathing through tubing, mouthpiece and one-way valves. It would have been very interesting to have measured end-tidal CO<sub>2</sub> as an indicator of the

extent of hypocapnia which may result from the chemically induced hyperventilation, but the equipment was not available during most of the study. Overall, the tachycardia is certainly the most dramatic of all the cardiorespiratory adjustments.

### Subjective effects of hypoxia (Box 5)

End-tidal CO<sub>2</sub> measures would be needed to distinguish the subjective effects of hypoxia from those evoked by hyperventilation-induced hypocapnia. The subjective experiences reported in this study are probably evoked by a combination of both hypoxia and hypocapnia, because the measured extent of hyperventilation was large enough to cause significant hypocapnia.<sup>6</sup>

Visual symptoms were most frequently described; 65% of subjects reported noticing at least one of the listed symptoms. Among the group of CNS and autonomic symptoms, headache

#### 4: Cardiorespiratory adjustments to reduced oxygen breathing (PO<sub>2</sub> equivalent to that at 25 000 feet altitude)

Subjects*	Duration of hypoxic exposure(s)	Mean pulse rate (beats/min)		Oxygen saturation at nailed bed (n = 138)		Brachial blood pressure (mmHg)		Minute ventilation volume (L/min) (n = 249)		Respiratory frequency (breaths/min) (n = 249)		Tidal volume of ventilation (L)	
		Start	End	Start	End†	Start	End	Start	End	Start	End	Start	End
All 452	259 ± 43	87	120	96%	52%	123/78	141/85	6.7	16.4	11.2	14.6	0.60	1.22
M 274	291 ± 46	82	115	96%	50%	128/79	145/88	7.4	17.5	11.0	13.8	0.67	1.27
F 178	217 ± 39	94	127	95%	53%	116/77	138/81	5.6	14.8	11.6	15.8	0.48	0.94

\*476 subjects commenced the procedure breathing air, but 24 (13 men, 11 women) withdrew early (before hypoxia) because of respiratory distress due to the resistance of the breathing equipment and are not included in the analysis. All subjects who completed the hypoxic exposure were cyanosed.

†Lowest SaO<sub>2</sub> at end of hypoxic exposure was 42%.

#### 5: Reported subjective effects of reduced oxygen breathing (hypoxic exposure equivalent to 25 000 feet) among 452 subjects

<b>Visual symptoms</b>	<b>295</b>	<b>(65%)</b>
Tunnel vision	152	(34%)
Colours reduced	124	(27%)
Blurred vision	61	(13%)
Scotoma	8	(1%)
<b>CNS/autonomic symptoms</b>	<b>299</b>	<b>(45%)</b>
Headache	169	(37%)
Dizziness, light-headedness	94	(21%)
Mental impairment or difficulty in concentration	87	(19%)
Euphoria	84	(19%)
Fading of ambient noises	82	(18%)
Anxiety or feelings of apprehension	42	(9%)
Flushing of face	39	(9%)
Tiredness, sleepiness	23	(6%)
<b>Neuromuscular symptoms</b>	<b>147</b>	<b>(38%)</b>
Sensory disturbances (eg, dysaesthesia, tingling)	98	(22%)
Motor incoordination	81	(18%)
Tremor	76	(17%)

#### 6: Observed neurological and cognitive effects of reduced oxygen breathing (hypoxic exposure equivalent to 25 000 feet) among 452 subjects

<b>Impaired memory functions</b>	<b>401</b>	<b>(89%)</b>
Impaired immediate recall	288	(64%)
Impaired delayed recall	213	(47%)
Impaired graphic memory (clock drawing)	84	(19%)
Semantic memory errors (proverbs)	82	(18%)
<b>Impaired computational functions</b> (simple arithmetic errors)	<b>207</b>	<b>(46%)</b>
<b>Impaired CNS decision/action functions</b> (perseveration [repetition] in writing or calculations)	<b>175</b>	<b>(39%)</b>
<b>Impaired visual-motor functions</b>	<b>113</b>	<b>(25%)</b>
Motor incoordination (illegible writing, poor drawing)	98	(22%)
Poor geometric figure reproduction	81	(18%)
Thought or motor block in writing or calculations	73	(16%)
<b>Neuromuscular symptoms</b> (tremor or muscle twitching)	<b>96</b>	<b>(21%)</b>

All subjects who completed the hypoxic exposure were cyanosed: the range of SaO<sub>2</sub> was 42%–61% when the observed impairments of cognitive function led to termination of the hypoxia.

was commonly reported and sometimes dizziness, light-headedness or difficulty in concentration. Some 18% of subjects reported noticing dullness or fading of ambient noises. In addition, euphoria was commoner than feelings of apprehension, with facial flushing, tiredness or drowsiness being reported less frequently. Subjects often described being aware of task commands, but feeling “powerless” to perform them — “as if the body would not obey the brain”. All these subjective effects are consistent with those previously reported to result from hypobaric hypoxia at altitude, well described in the US Army Field Manual<sup>5</sup> and by Ernsting.<sup>1,6</sup> However, the relative frequency of the symptoms reported in this study is of interest and may reflect the medical or paramedical background of the participating volunteers.

### Neurological and cognitive effects of hypoxia (Box 6)

Many subjects (89%) showed disturbances of memory functions, with serial 7 subtractions (immediate recall) being the single most prevalent abnormality (64%). The tests of delayed recall of a name and address and 7 digit number were also frequently impaired (47%), but graphic and semantic memory showed less frequent errors. Simple arithmetical errors were made by 46% of subjects. Perseveration was also a common finding (39%). Visual-motor coordination was impaired in 25% of subjects, who exhibited motor incoordination, jerkiness, illegible writing and poor reproduction of geometric figures. It is noteworthy that only 16% of all subjects volunteered a reported thought block or complained that they could not complete a written task they were instructed to do. This is in contrast to more than 50% who admitted this on interrogation when their worksheets were discussed with them. This may be explained by some persistent memory or concentration impairment immediately following the hypoxia, or suggestibility during the post-hypoxia interrogation. Neuromuscular symptoms of tremor or twitching were noted in 17% of subjects.

People in the late stage of hypoxia, preceding unconsciousness, lapse into a semi-conscious state, mentally switched off and unresponsive, with eyes open and head upright.<sup>6</sup> The protocol in this study required return to normal air breathing as soon as at least two errors in cognitive function had been detected, and no subjects reached this stage. However, subjects often described feeling unable to execute commands, or feelings of euphoria or carelessness, which cast doubt on the ability of these individuals to respond to an emergency in hypoxic conditions.

The concept of “time of useful consciousness” was well illustrated to participants in this hypoxia familiarisation study because the duration of the hypoxic exposure (259 ± 43 s) corresponded to the time at which they had made at least two errors on the cognitive function tests. The difference observed in time of useful consciousness between men and women was statistically significant ( $P < 0.05$ ) and may be explained by differences in body weight, with men having a greater dissolved oxygen reserve in body fluids, or higher blood haemoglobin

concentration. A recent review of time of useful consciousness and pressure changes with altitude is given by Wolff.<sup>7</sup>

The correlations drawn here between cognitive deficits and duration of hypoxic exposure provide a method of roughly estimating the “time of useful consciousness” in participating subjects. Computer-assisted tests of cognitive function are now available,<sup>8</sup> including a short version of Cogstate suitable for testing footballers suffering concussion, and these are likely to prove useful in studies of hypoxia, fatigue or other conditions likely to produce subtle cognitive deficits.

## Conclusions

This study used a reduced oxygen gas mixture (6%–7% oxygen) to achieve normobaric hypoxia simulating an altitude of 25 000 feet. It illustrates the variability of physiological responses, subjective symptoms and cognitive effects of hypoxia in healthy volunteers. Using the reduced oxygen breathing procedure in small groups, where participants also took part as observers, provided a clear demonstration of the insidious onset and obvious performance deficits resulting from hypoxia.

Altitude simulation using such a reduced oxygen breathing technique provides a safe, convenient and cost-effective way to familiarise medical and paramedical personnel and aviators with the potentially dangerous effects of hypoxia, their individual response to it, and the brevity of the time of useful consciousness available in an emergency under hypoxic conditions.

## Acknowledgements

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