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Effects of normobaric hypoxic confinement on human performance

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Title

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Abstract

Because of the ban on production and use of halons replacement agents or other methods are needed for fire extinguishing. The technique of reduced oxygen levels has attracted great interest both in regard to fire extinguishing as well as for fire prevention in closed spaces such as for instance submarines. However, if humans are to work and live in environments with reduced oxygen levels, the effects of hypoxia on human performance must be further assessed.

In three 11- to 14-day confinements a total of 22 subjects were exposed to different levels of normobaric hypoxia (14 and 15 kPa O_2, for up to 10 days, and 13 kPa for 24 hr) with intervening periods of normoxia. In each experiment eight subjects were divided into two teams, working in six hour shifts around the clock, as practiced onboard Swedish submarines. Physiological, cognitive, psychomotor, and motor performance tests, and questionnaires were administered once or twice in every 24-hour period.

All of the subjects appeared to tolerate the acute reduction in oxygen partial pressure well. In many of the tests performance improved with time as a result of learning, despite reductions in the oxygen level. No reduction in cognitive or psychomotor performance or learning was observed at any of the oxygen levels tested.

Oxygen levels down to 14 kPa was well tolerated for up to 10 days. Cognitive and psychomotor performance was maintained during 24 h long exposures to 13 kPa oxygen, but exposure to this level of hypoxia caused an increase in subjective symptoms.

Key words
acclimatization, cognitive performance, hypoxia, physical performance, psychomotor performance,

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Effects of normobaric hypoxic confinement on human performance.

Huvudinnehåll

Förbudet att använda halon för brandsläckning gör att nya metoder måste utarbetas. Sänkt oxygenhalt som brandförebyggande åtgärd i slutna utrymmen, t ex ubåtar har rönt stort intresse. Om människor skall leva och arbeta i atmosfär med sänkt oxygenhalt måste dess påverkan på mental och fysisk prestationsförmåga utvärderas.

Tre försök, 11 till 14 dagar långa har genomförts, med totalt 22 personer som exponerats för sänkt oxygenpartialtryck men med normalt atmosfärstryck (normobar hypoxi med 13, 14 och 15 kPa O_2) upp till 10 dagar med mellanliggande normoxi perioder (21 kPa O_2). I varje experiment har de åtta försökspersonerna varit indelade i två team vilka arbetat efter samma 6-timmars skiftsystem som ombord på svenska ubåtar. Fysiska, kognitiva, psykomotoriska och motoriska tester samt besvarande av frågeformulär har genomförts en eller två gånger under varje 24-timmars period.

Försökspersonerna tolererade sänkningen av oxygenpartialtrycket väl. I många tester förbättrades resultaten med tiden som en effekt av inlärning även vid hypoxi.

10 dagars vistelse i atmosfär med oxygenpartialtryck ner till 14 kPa påverkade inte försökspersonerna nämnvärt. Den kognitiva och psykomotoriska prestationsförmågan bibehölls även vid dygnslång exposition för 13 kPa oxygen men ledde till en ökning i skattning av subjektiva symptom.

Nyckelord
acklimatisering, fysisk prestation, hypoxi, kognitiv prestation, psykomotorisk prestation

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SUMMARY

Because of the ban on production and use of halons replacement agents or other methods are needed for fire extinguishing. The technique of reduced oxygen levels has attracted great interest both in regard to fire extinguishing as well as for fire prevention in closed spaces such as for instance submarines. However, if humans are to work and live in environments with reduced oxygen levels, the effects of hypoxia on human performance must be further assessed.

In three 11- to 14-day confinements a total of 22 subjects were exposed to different levels of normobaric hypoxia (14 and 15 kPa O_2, for up to 10 days, and 13 kPa for 24 hr) with intervening periods of normoxia. In each experiment eight subjects were divided into two teams, working in six hour shifts around the clock, as practiced onboard Swedish submarines. Physiological, cognitive, psychomotor, and motor performance tests, and questionnaires were administered once or twice in every 24-hour period.

All of the subjects appeared to tolerate the acute reduction in oxygen partial pressure well. In many of the tests performance improved with time as a result of learning, despite reductions in the oxygen level. No reduction in cognitive or psychomotor performance or learning was observed at any of the oxygen levels tested.

Oxygen levels down to 14 kPa was well tolerated for up to 10 days. Cognitive and psychomotor performance was maintained during 24 h long exposures to 13 kPa oxygen, but exposure to this level of hypoxia caused an increase in subjective symptoms.

1 INTRODUCTION

Halons have proven to be efficient compounds for use in fire extinguishing systems. However, due to the contamination of the global atmosphere the use of halons are to be phased out. New fire extinguishing systems are thus needed (Berg & Godby,1993). As most substances will not burn if the oxygen fraction is lower than 14 %, rapid reduction of the oxygen fraction in air, through dilution with inert gas mixtures, has been introduced as a fire fighting technique (Carhart & Gann, 1974; Cook, Dorr, & Shields, 1968; Lambertsen, 1994 (a); Lambertsen, 1994 (c)). Reduced oxygen levels can also be used for fire prevention in confined and air tight spaces, where a stable atmosphere can be maintained (Knight, 1985). Such a method to achieve fireproofing could be utilized in submarines, computer halls, control rooms, storage rooms, museums, archives or other facilities where water sensitive items and equipment have to be protected against fire and toxic and corrosive combustion products. The problem of using gas mixtures with low oxygen content in fire fighting and fire protection is that hypoxia may effect humans present.

Exposure to low levels of oxygen (hypoxia) is relevant in many fields: In aviation medicine, cognitive, visual and motor performance as well as physiological effects of exposures to acute hypobaric hypoxia is of interest (for a review see Ernsting & King, 1994), in sports medicine physical performance and mechanisms of acclimatization to moderate levels of hypobaric hypoxia have been studied (Bhattacharjya, 1964; Bro-Rieskov, 1986); and in alpine or mountaineering medicine both acclimatization and physical and mental performance at extremely low oxygen levels have been investigated (Cymerman & Rock, 1994; West & Lahiri, 1984).

However, the performance during extended exposure to moderate levels of normobaric hypoxia in so called "fire retardant atmospheres" has not been given as much attention as hypobaric hypoxia. One relevant study on normobaric hypoxia was carried out at The Naval Submarine Base in Grotton, USA (Knight et al, 1990; Schlichting, Knight, Cymerman, 1988; Shukitt et al, 1988). Performance at two levels of normobaric hypoxia was studied, 13 and 17 % O_2, and to simulate the conditions aboard submarines the atmosphere was "contaminated" with 0.9 % CO_2. From this study it was concluded that normobaric 17 % O_2 was acceptable, but normobaric 13 % O_2 produced short-term decrements in cognitive functioning and mood, lasting a day or so, and moderate symptoms of acute mountain sickness in some individuals.

In submarines with diesel-electrical propulsion hypoxic atmospheres can not easily be established because fresh air is sucked into the boat each time snorting is performed to charge the batteries. However in nuclear powered submarines, and in the next generation of Swedish submarines, equipped with air independent Stirling machinery (Kockums Type A 19, Gotland-class), stable atmospheres can be maintained for much

longer periods. The method of fire prevention through oxygen reduction will therefore become a possible concept for fire prevention in the next generation of Swedish submarines. The use of liquid oxygen (LOX) as oxidant for the Stirling engine, with the concomitant risk of sudden release of large amounts of oxygen, is an additional reason for studying flame-retardant atmospheres with low oxygen content.

If humans are to work and live in localities where hypoxic atmospheres are used, a balance must be struck between the level of fire prevention achieved and the effect of hypoxia on human performance. The magnitude of these effects must therefore be carefully evaluated before fire retardant atmospheres can be used in confined spaces where humans are working.

The purpose of this study was to increase the knowledge on human physiological, cognitive, and psychomotor performance in normobaric hypoxia, or "fire retardant atmospheres." For this reason normobaric hypoxic exposures to 13, 14, and 15 kPa O_2 lasting up to 10 days were carried out.

The test protocol included performance on approximately 20 cognitive, psychomotor, and motor tests and a number of questionnaires concerning mood, symptoms of acute mountain sickness, sleep quality, sleep length, and personality dimensions. At rest and during physical exercise on a bicycle ergometer, measurements of cardio-respiratory parameters were carried out. Measurements of optical readaptation time, fatique, hand grip strength, body weight, body temperature, cardiac dimensions, and blood parameters were also included in the physiological test protocol.

The effects of hypoxia on cognitive, psychomotor, and motor performance and submaximal work capacity at low levels were measured and the aim of the three studies was to find the lowest possible oxygen partial pressure at which cognitive, psychomotor, and motor performance are unaffected.

2 EFFECTS OF REDUCED OXYGEN LEVELS

2.1 PHYSICAL EFFECTS OF REDUCED F_{O2}

Combustion or burning can be defined as a chemical and physical reaction between a fuel and oxygen that generates heat. Apart from heat, combustion also usually produces light, smoke, and combustion gases. Three conditions are necessary to have a fire: a fuel must be present, it must be in contact with oxygen, and there must be a source of energy to raise the temperature of the fuel and oxygen to a point where they start to react rapidly - i.e. to ignite.

2.1.1 Relationship between oxygen fraction and fire

Since oxygen combines with fuel in the combustion process, the size of a fire may be limited by either the amount of fuel available or by the amount of oxygen which can reach the fire (Brannigan, Bright, & Jason, 1980). Thus, a fire in a tightly-closed compartment will go out when the oxygen concentration drops. The strong relationship between oxygen fraction (F_{O2}) and fire characteristics such as burning rate is illustrated in Figure 1 and Figure 2.

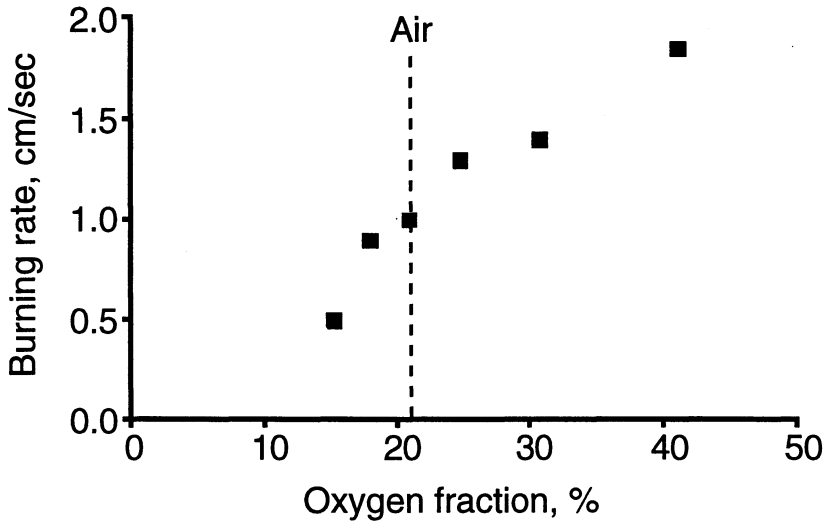


Figure 1. *Burning rates of filter paper strips (angle 45°, pressure 100 kPa) in different oxygen fractions (F_{O2}) serve as an example of the strong relationship between burning rate and F_{O2} (Redrawn from Schmidt, Dorr, & Hamilton, 1973). Note that at 100 kPa (1 atm) the figures for F_{O2} (%) and for oxygen partial pressure (P_{O2}, kPa), are almost the same.*

In a fire retardant atmosphere the increased number of inert gas molecules affects fire properties by being a physical obstacle to the effective interaction of a fuel and oxygen molecules. The number of inert gas molecules interfere with this rection in at least three ways: by promoting reaction chain termination, by promoting the formation of free radicals which do not lead to branching chain reaction propagation, and by cooling the reaction and the reactants (Schmidt, Dorr, & Hamilton, 1973).

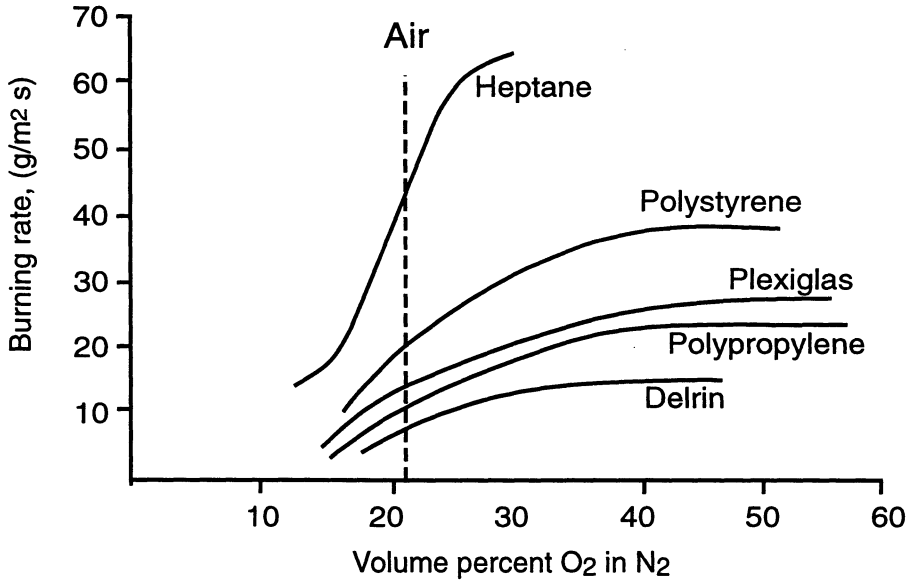


Figure 2. *Effect of oxygen percentage on the burning rate for heptane and small, thin, horizontal samples of plastics. From Tewarsson (1988).*

Another way to illustrate the impact of F_{O_2} on combustion is the oxygen index value. The oxygen index value is defined as the lowest fraction of oxygen that will just barely support propagation of combustion for a given substance (at 100 kPa). In Table 1 oxygen index values for some common materials are listed.

Table 1. *Oxygen Index Values for some common materials.*

Material	Oxygen index value
Methanol	11.0 - 12.0
Acetone	16.0
Cotton	16.0 - 18.5
Mineral oil	16.1
Paper, cellulose filter	18.2
Polyester fibres	20.6
Wool	23.8

The values in the table were determined using the ASTM Oxygen test (D2863)(Quincy, 1986).

In view of the above, parallel to the investigation on human performance, the Swedish Defence Research Establishment has, on request from the Swedish Defence Material Administration, started an investigation on ignition, burning and combustion products in atmospheres with 15 and 21 % O_2. These tests have been carried out on materials approved for use on board Swedish submarines. Results from these tests are presented in Table 2. For three of the materials the thermal irradiation limit for "pilot ignition" was found to be 20-60 % higher in 15 % than in 21 % O_2 at normal pressure (Werling & Onnermark, 1994).

Table 2. *Thermal irradiation limit for "pilot ignition" (W/cm2).*

Material	**21 %**	**15 %**	**Δ**
Hydraulic oil	0.35	0.35	0 %
Tarkett (4 mm plastic foil on steel plate)	1.5	1.5	0 %
Cable (plastic insulated)	2.9	3.5	+ 20 %
Isolamin (0.15 mm plastic foil on steel plate)	2.5	3.9	+ 56 %
Diesel oil	0.25	0.4	+ 60 %

Data from Werling and Onnermark, 1994.

When organic fuels burn with an abundant supply of oxygen the principal products are water, carbon dioxide (CO_2) and some carbon monoxide (CO). When the oxygen supply is limited, combustion will be incomplete and the ratio of CO to CO_2 increases as the O_2 supply is decreased. CO is highly toxic and a concentration of 3000 ppm can cause death in half an hour (Brannigan et al, 1980).

Apart from the supposed negative effects on human performance in atmospheres with low F_{O2} the aspects of incomplete combustion and accompanying increase in toxic combustion products have to be considered in case of fire.

2.1.2 Fire prevention

There are different methods and techniques to manipulate the oxygen content or concentration in order to achieve a fire retardant atmosphere in a closed space e.g. a submarine:

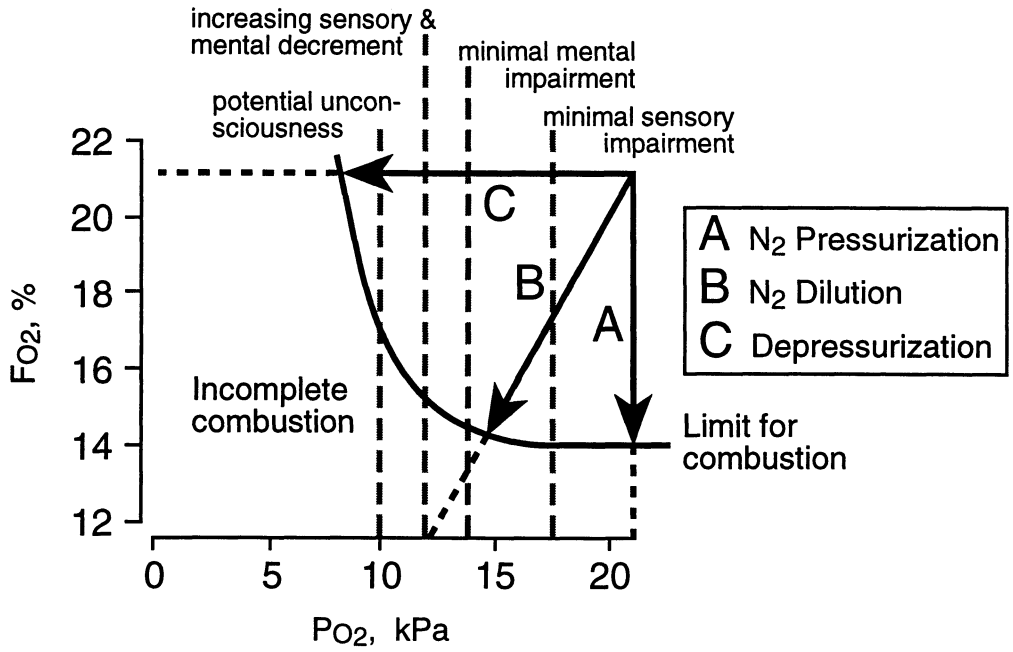


Figure 3. *Potential modifications of air. Redrawn from Knight (1991). The solid arrows represent modifications of the atmosphere at sea level that will produce a flame suppressant atmosphere. Atmospheric conditions on or below the curve do not support the complete combustion of paper strips. Limits for sensory and mental impairment is adapted from McFarland (1970).*

A. Pressurization with inert gas (see Figure 3, arrow A). To lower the F_{O2} of air to 15 % with an unchanged P_{O2} the pressure will have to be increased to approximately 140 kPa (1.4 atm) by addition of inert gas e.g. nitrogen (N_2). Even if a 85/15 N_2/ O_2 atmosphere at 140 kPa has a slightly lower nitrogen content than air at 160 kPa, which is the largest pressure that allows direct ascent to the surface after unlimited exposure, the pressure increase still would constitute a definite risk for decompression illness. Furthermore, it increases the risks of decompression illness in case of later free ascent rescue manoeuvre.

B. Dilution with inert gas at normobaric pressure (see Figure 3, arrow B). The total pressure is kept unchanged while P_{O2} and F_{O2} is allowed to drop gradually, when the oxygen is consumed by the crew. The pressure is kept constant through addition of N_2. A more rapid decrease in F_{O2} can be achieved through addition of pure nitrogen and ventilation of excess gas (compare fire extinguishing chapter 2.1.3). This requires storage of larger quantities of N_2.

C. Depressurization through air evacuation (see Figure 3, arrow C). Air evacuation leads to a decrease in the total pressure and in the P_{O2}, but the F_{O2} remains unchanged. In order to achieve the same fire proofing effects as with pressurization and dilution, P_{O2} will have to reach levels that are unacceptable for humans.

In principle the techniques that could be used are, pressurization or dilution with inert gas. In a closed space oxygen can also be extracted by human metabolism or other controlled oxygen extraction.

2.1.3 Fire extinguishing

Presently two different agents are commercially available for the fire extinguishing by reduction of F_{O2}: INERGEN ™ (Wormald, Fire Systems AB, Sweden), and ARGONITE ® (Premo Security AB).

Argonite contains argon (Ar) and nitrogen (N_2) in equal parts and Inergen, contains 40 % Ar, 52 % N_2 and 8 % CO_2. These gas mixtures should be added rapidly to the atmosphere surrounding the fire giving an oxygen concentration that is reduced to about 12-15 %. The CO_2 addition in Inergen gives an advantage in counteracting hypoxia effects (Gibbs, Gibbs, & Lennox, 1943, Lambertsen, 1994 (a)). However, if this method is to be used for fire fighting the homogeneity of the fire extinguishing atmosphere has to be considered.

2.2 BIOLOGICAL EFFECTS OF REDUCED P_{O_2}

As mentioned earlier combustion is influenced by the oxygen fraction (F_{O_2}). Human life-processes on the other hand depend on the partial pressure of oxygen (P_{O_2}). In humans, decreased P_{O_2} in the atmosphere leads to hypoxia which can be defined as the state in which P_{O_2} in lungs, blood, and /or tissue is low compared with a healthy person at sea level breathing air. There is a fairly good tolerance to changes in the oxygen partial pressure which means that one can travel and stay at relatively high altitude without any serious symptoms of hypobaric hypoxia or mountain sickness.

In fire retardant submarine atmospheres the problem which has to be considered is normobaric hypoxia. Oxygen partial pressure as well as F_{O_2} is decreased while total pressure is kept equivalent to sea level pressure (1 atm or 100 kPa). Note that at normobaric pressure or at sea level pressure the figure for P_{O_2} and F_{O_2} are almost the same.

To be able to compare results from mountain sojourns, simulated hypobaric, and normobaric hypoxic exposures the inspired oxygen partial pressure has to be compared.

Different methods has been used to recalculate altitude from measures of atmospheric pressure (West, 1996). In this report comparison between altitude figures and oxygen partial pressure have been made with the barometric formula. The relationship between P_{O_2} and altitude is illustrated in Figure 4.

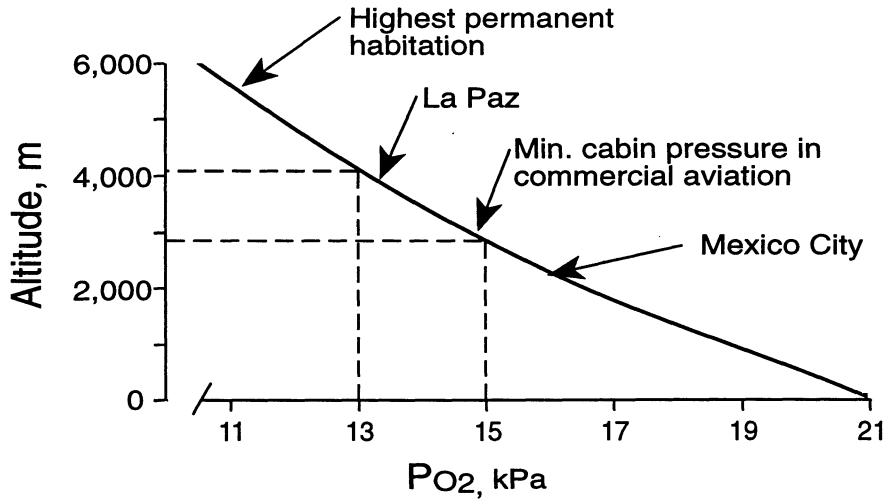


Figure 4. *Relationship between oxygen partial pressure (P_{O_2}) and altitude as plotted from the "Barometric formula" (Nordling & Österman, 1985). Note that at sea level or normobaric pressure the figures for P_{O_2} (kPa) and oxygen fraction, F_{O_2} (%) are almost the same. Broken lines indicates P_{O_2} levels used in this study (13 to 15 kPa O_2 at normobaric pressure).*

However it should be kept in mind that the resulting hypoxia while breathing air at altitude will be more severe than breathing a gas mix with the same P_{O2} at normobaric pressure. The resulting alveolar oxygen pressure will be lower at hypobaric pressure since the alveolar oxygen partial pressure of water vapor and CO_2 will remain unchanged and take a greater proportion of the total pressure at high altitude (discounting any hyperventilation). See Figure 5.

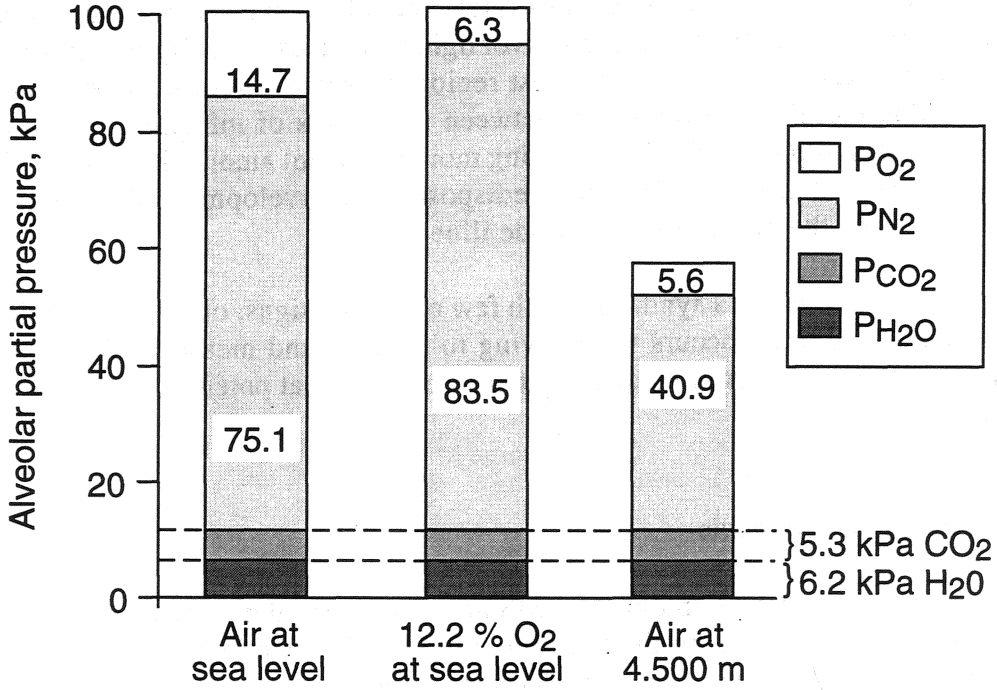


Figure 5. *Alveolar partial pressure of H_2O, CO_2, N_2 and O_2 during normoxia (at sea level breathing air, 21 % O_2, $P_{O2} \approx 12.2$ kPa), during normoaric hypoxia (at sea level breathing 12.2 % O_2,), and during hypobaric hypoxia (4,500 m breathing air, 21 % O_2, $P_{O2} \approx 12.2$ kPa). Redrawn from Le Pechon, 1994.*

2.2.1 Subjective symptoms

2.2.1.1 Hypobaric hypoxia

When exposed to high terrestrial altitude a cascade of physiological changes are initialized in order to compensate for the lack of oxygen. Due to the combination of these reactions and the inability of the body to fully compensate for the reduced ambient oxygen concentration when exposed to hypoxia a number of symptoms and signs will appear, usually called Acute Mountain Sickness (AMS). This syndrome can be defined as "a subjective experience of feeling sick while exposed to high terrestrial

altitude of approximately 2,400 m or greater (less than approximately 16 kPa O_2) with other attributable causes of illness ruled out" (Sampson et al, 1983).

AMS can appear within hours to days of reaching altitude and the incidence and severity of symptoms vary with the initial altitude, the rate of ascent, the level of exertion during ascent or within the first 24 hours after ascent, and there is also a great individual susceptibility. The most common symptoms are headache, anorexia, nausea and vomiting. Other symptoms and signs include weakness, lassitude, general malaise, decreased coordination, dizziness or lightheadedness and oliguria. In a recent study among hikers in the Mount Everest region of Nepal (Murdoch, 1995) it was suggested that there is an association between symptoms of infection and altitude illness, with all symptoms of infection being more prevalent among those with AMS. He concluded that if infections does not predispose to the development of AMS, it may at least aggravate the symptoms of altitude illness.

Mild to moderate AMS is a syndrome with few objective signs, other than vomiting. Thus, a major difficulty occurs when trying to identify and measure AMS. Of the procedures available, structured questionnaires offer a great potential for systematic measurement.

2.2.1.2 Normobaric hypoxia

It has been reported that symptoms of AMS are less severe and more delayed during normobaric hypoxic exposure than during simulated hypobaric hypoxic exposure, even though P_{O2} of the inspired gas (P_{IO2}) is the same (Roach, Loeppky, & Icenogle, 1996). As mentioned earlier in this report (chapter 2.2), this can be due to the fact that hypobaric hypoxic exposures result in lower alveolar oxygen partial pressures than do normobaric hypoxic exposures even though P_{IO2} are equivalent.

2.2.2 Physiological response

2.2.2.1 Hypobaric hypoxia

The short-term acclimatization or the physiological changes that help to maintain oxygenation of the tissues during hypobaric hypoxia (Cymerman & Rock, 1994; Denison, 1981; Ernsting & King, 1994) can be divided into three phases (Bro-Rieskov, 1986). It must be noted that the level of hypoxia as well as the large individual variations makes any classification indistinct and makes the borders between the phases non-distinct.

0-1 day of hypobaric hypoxia (acute hypoxia)
Increased heart rate during both rest and submaximal exercise and increased ventilation are the momentary responses to hypoxia. After that increased erythropoietin levels and decreased plasma volume are seen.

The oxygen saturation of haemoglobin is essential to the oxygenation of the tissues. The oxygen-haemoglobin dissociation curve (see Figure 6) illustrates the relationship between oxygen partial pressure and the oxygen saturation of haemoglobin (S_{aO_2}). Some conditions in the blood that changes the Hb affinity for oxygen, and shifts the curve along the x-axis are temperature, pH and the concentration of 2,3-diphosphoglycerate (2,3-DPG). A temperature increase or a fall in pH, shifts the curve to the right causing higher P_{O_2} to be required to bind a given amount of O_2. Conversely when the temperature falls and pH rises the curve shifts to the left and the P_{O_2} required to bind the same amount of O_2 is lower. When the amount of 2,3-DPG increases the curve shifts to the right.

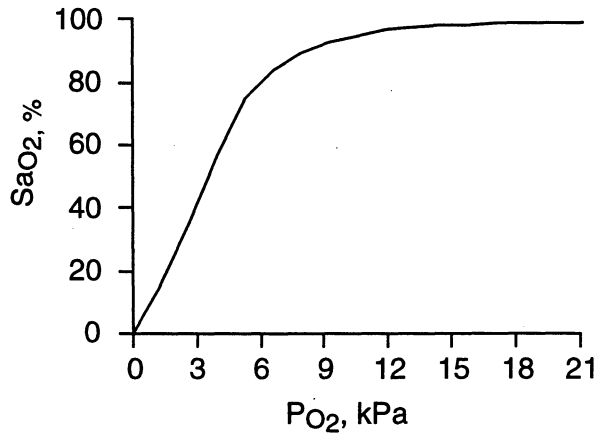


Figure 6. Oxygen-hemoglobin dissociation curve. (From Comroe. Physiology of Respiration, 2nd ed. Copyright © 1974, Year Book Medical Publishers Inc.)

Decreased P_{O_2} of the inspired gas stimulate peripheral chemoreceptors located in the carotid artery to increase ventilation and thereby raise the P_{O_2} and decrease P_{CO_2} in the alveoli resulting in respiratory alkalosis and a rise in the blood pH. The Hb-dissociation curve shifts to the left giving Hb affinity for O_2 to increase.

Increased erythropoietin levels in the blood triggers the production and release of red blood cells from the bone marrow. Erythropoietin (epo) is a circulatory glucoprotein that is produced in the kidneys and in the liver. As O_2 delivery is diminished epo production and release to the circulation is increased (Eckhardt et al, 1989).

Within hours of ascent there is a decrease in plasma volume caused by fluid shifts from the intravascular space to the interstitial and/or the intracellular space (Rock et al, 1993). This gives a relative increase in hemoglobin concentration and effective oxygen carrying capacity of the blood without an absolute increase in red cell number.

1-7 days of hypobaric hypoxia
Further increased ventilation and increase in 2,3-DPG levels in the blood is seen. To compensate for the respiratory alkalosis caused by hyperventilation excretion of bicarbonate from the kidneys is increased. All this shifts the O_2-haemoglobin dissociation curve to the right and oxygen transport to the tissue increases (see Figure 6).

Haemoglobin synthesis is enhanced and the increased release of red blood cells from the bone marrow can be seen after 2-3 days, but, it is not until several weeks later that this increase has an impact on the O_2 carrying capability. Erythropoietin concentration and heart rate at rest will return to normal levels.

More than 7 days of hypobaric hypoxia
Triggered by the initially high erythropoietin concentration the number of new red blood cells will increase further and plasma volume will slowly approach sea level volumes. The ventilation is stabilized to a level just above that at sea level. Pulse rate is the same as after 1 to 7 days and the increase in cardiac output seen initially is decreased, but, will not be reduced to sea level values.

In the muscles an increased number of capillaries and an increase in myoglobin is seen, this leads to improved O_2 diffusion to the muscle cells and increased O_2 storing capacity in the muscle.

2.2.2.2 Normobaric hypoxia

Acute normobaric hypoxia
Fire suppression through inert gas dilution, using gas mixtures like Inergen® or Argonite™, will expose people present to acute normobaric hypoxia which gives respiratory stimulation and a reduction of arterial and brain carbon dioxide partial pressure. The hypocapnia reduces the cerebral blood flow which further reduces the oxygen delivery. By providing increased inspiratory carbon dioxide acute adaptation to hypoxia is obtained. This acute adaptation prevents loss of respiratory stimulus, increase arterial oxygenation, improve blood flow to brain and other tissues, and restore brain tissue carbon dioxide (Lambertsen, 1994 (c)).

Lambertsen (1994 (b)) showed that the effects of acute exposure to normobaric hypoxic atmospheres (5-8 % oxygen) could be overcome by the addition of carbon dioxide to the gas mixture, and concluded that such a gas could be used to extinguish fires in closed spaces even if occupied by humans.

More than 1 day in normobaric hypoxia
If "fire retardant atmospheres" are used humans may work and live from hours to weeks in an atmosphere with reduced oxygen partial pressure/oxygen fraction.

As mentioned earlier in this report Roach, Loeppky, & Icenogle (1996) has reported a distinction in severity between the physiological response to normobaric and hypobaric hypoxia, with less severe symptoms in normobaric hypoxia.

2.2.3 Effects on sense organs

The central nervous system and the retina are the organs that are most sensitive to hypoxia. The first signs of hypoxia are thus visual impairment followed by decrement in cognitive and motor performance.

It was found that dark adaptation was delayed at an altitude of 1,200 m (approximately 18 kPa O_2). However these effects were thought to have no consequence in relation to night blindness in pilots until altitudes above 3,000 m (McFarland & Evans, 1939, McFarland 1971). Anecdotally the loss of arterial oxygen saturation at 2,300 m ($\approx$ 16 kPa O_2) is similar to that from smoking three cigarettes (McFarland, 1970) and absorption of the similar amount of CO at 2,300 m causes a loss of light sensitivity similar to that above 3,000 m (> 14.7 kPa O_2).

Mild hypoxia (3,500 m, $\approx$13.9 kPa O_2) also results in an initial increase in V wave latency, during auditory brainstem evoked response (ABER), corresponding to a decrease in auditive sensitivity. With prolonged exposure the sensitivity recovered which suggest that the auditory system can compensate for mild hypoxia. (Carlile & Paterson, 1992). Hypoxia (12 % O_2) has been shown to have no effect on speech recognition in noise (Marshall, 1987).

2.2.4 Effect on cognitive, psychomotor and motor performance

There are conflicting results in the literature regarding the effect of hypoxia on cognitive and motor performance. With an inspiratory oxygen partial pressure (P_{IO_2}) lower than approximately 17 kPa O_2 a number of authors have reported impaired learning and impaired performance. In Table 3 are shown exemples of experiments that have yielded results showing impaired performance at P_{IO_2} between 17.6 and 11.7 kPa. However, there are also reports stating unaffected performance if the oxygen partial pressure was higher than approximately 13 kPa. Table 4 show examples of tests in which performance was unimpaired or even improved at similar hypoxic levels. Note that the resulting hypoxia while breathing air at altitude will be more severe than breathing gas mix with the same P_{IO_2} at normobaric pressure (chapter 2.2, page 17).

Table 3. *Hypoxic conditions at which impaired performance on different tests has been observed.*

Altitude (m)	≈ P_{IO_2} (kPa)	Type of test	Reference
1,524	17.6	spatial orientation	Denison et al, 1966
2,133	16.3	reaction time	Ledwith, 1970
2,133	16.3	visual orientation (RT)	McCarthy et al, 1995
2,440	15.7	vigilance	Kelman & Crow, 1969
2,440	15.7	spatial orientation	Farmer et al, 1992
0 ‡	14.8	serial choice RT	Fowler et al, 1987
3,048	14.7	response time	Ledwith, 1970
3,048	14.7	aritmetics	Vaernes, 1984
"	"	reasoning	"
"	"	long term memory	"
"	"	perceptual speed	"
"	"	visual RT	"
"	"	hand wrist speed	"
3,600 *	13.7	rate of information processing	White, 1984
" *	"	memory	"
3,657	13.6	visual orientation (judgement)	McCarthy et al, 1995
3,660	13.6	logical reasoning	Green & Morgan, 1985
0 ‡	13.0	computer interaction	Shukitt et al, 1988
4,300	12.7	Stroop, interference	Crowley et al, 1992
"	"	code substitution	"
"	"	logical reasoning	"
4,559 *	12.3	STM, digit span forward	Regard et al, 1991
" *	"	figural memory, error rate	"
4,790 *	11.9	reaction time	Mackintosh et al, 1988

The inspiratory oxygen partial pressure (P_{IO_2}) that corresponds to the given altitude has been calculated using the barometric formula (see chapter 2.2).
All exposures are simulated hypobaric exposures in pressure chamber except for those marked:

* Mountain sojourn

‡ Normobaric hypoxic exposure

Table 4. Hypoxic conditions at which unchanged performance on different tests has been obseerved.

Altitude (m)	≈	P_{IO_2} (kPa)	Type of test	Reference
2,133		16.3	visual orientation	McCarthy et al,1995
0	‡	17.0	computer interaction	Shukitt et al, 1988
2,438		15.7	spatial orientation	Fowler et al, 1985
2,438		15.7	short-term memory	Crow & Kelman, 1971
3,048		14.6	hidden patterns	Vaernes, 1984
"		"	operational tests	"
"		"	finger dexterity	"
3,050		14.6	logical reasoning	Green & Morgan, 1985
3,600	*	13.7	trail making	White, 1984
"	*	"	letter-digit code	"
"	*	"	dual task cancellation	"
"	*	"	subtraction	"
3,658		13.6	spatial orientation	Paul & Fraser, 1994
"		"	serial choice RT	"
"		"	logical reasoning	"
0	‡	13.0	addition	Shukitt et al, 1988
"	‡	"	coding	"
"	‡	"	map/compass	"
"	‡	"	number comparison	"
"	‡	"	pattern comparison (paper)	"
"	‡	"	pattern comparison (computer)	"
"	‡	"	pattern recognition	"
4,300		12.7	serial addition/subtraction	Crowley et al, 1992
"		"	letter search	"
"		"	4-choice reaction time	"
"		"	spatial orientation	"
"		"	delayed recall	"
"		"	matching sample	"
4,559	*	12.3	Rey verbal learning	Regard et al, 1991
"	*	"	STM, digit span backward	"
5,000	*	11.7	alertness	Mackintosh et al, 1988

The inspiratory oxygen partial pressure (P_{IO_2}) that corresponds to the given altitude has been calculated using the barometric formula (see chapter 2.2).
All exposures are simulated hypobaric exposures in pressure chamber except for those marked:

* Mountain sojourn

‡ Normobaric hypoxic exposure

2.2.4.1 Simulated hypobaric hypoxia (in pressure chamber)

In 1966 Denison, Ledwith, and Poulton concluded that the altitude threshold for deterioration in mental functions may be as low as 1,524 m (≈ 17.6 kPa O_2), based on performance on a spatial orientation task (Manikin). Acute hypoxia appeared to affect the early stages of learning but did not reduce performance once the task had been learned. Similar results were published by Farmer et al (1992) who found that mild acute hypoxia (≈ 15.7 kPa O_2) both degraded performance and inhibited learning of the Manikin task and that the initial performance decrement persisted even during subsequent performance of the task under controlled conditions. On the other hand Paul and Fraser in 1994 reported that the ability to learn new tasks like spatial orientation (Manikin), serial choice reaction time, and logical reasoning (Baddeley) was not impaired by mild acute hypoxia at simulated altitudes of up to 3,658 m (≈ 13.6 kPa O_2).

From an experiment with acute exposure to a simulated altitude of 3,048 m (≈ 14.7 kPa O_2) Vaernes, Owe, and Myking (1984) reported impaired performance on seven out of nine different neuropsychological and operational tests. Testing was performed on reaching 3,048 m and every second hour for 6.5 h. Apart from impaired performance subjects in this study reported headache, weakness, and some dizziness.

Green and Morgan (1985) introduced a logical reasoning task (Baddeley) to five independent groups of subjects at different altitudes to determine the effect of hypoxia on learning. No difference in the learning rate of the task was seen in the different groups, but the subjects tested at 3,600 m (≈13.8 kPa O_2) had a significantly higher error rate compared to the groups tested at 0, 305, 2,440, and 3,050 m (≈ 21, 20.3, 15.8, and 14.7 kPa O_2 respectively).

From performance on a vigilance task Kelman and Crow (1969) concluded that acute exposure to a simulated altitude of 2,438 m (≈ 15.7 kPa O_2) impairs learning of a new task. Simulated altitudes of 609 m and 2,438 m on the other hand had no demonstrable effect on human short-term memory (Crow & Kelman, 1971).

Response time on a task concerning the orientation of a visual stimuli was found to be significantly slower at acute exposures to simulated altitudes of 2,133 m and 3,657 m (16.3 and13.6 kPa O_2 respectively) compared to sea level (MacCarthy et al, 1995). A signal detection analysis showed that accuracy of judgement were significantly poorer at 3,657 m compared to 2,133 m and sea level. Ledwith (1970) found that from ground level to 2,133 or 3,048 m (≈ 16.3 and 14.7 kPa O_2) reaction time increased and movement time decreased significantly for naive subjects.

After rapid ascent to a simulated altitude of 4,300 m (≈12.7 kPa) performance in some aspects of memory, grammatical reasoning, and Stroop tests was significantly impaired, but all these effects subsided by the end of the first day at altitude (Crowley et al, 1992).

Mackintosh et al (1988) found that mean reaction time increased in subjects with marked symptoms of acute mountain sickness (AMS), whereas the alertness tests showed no effects. The tests used were simple reaction time and alertness at 5,008 m and a three choice reaction time test at 4,790 m (≈11.6 and 11.9 kPa O_2).

2.2.4.2 Hypobaric or altitude hypoxia (mountain sojourn)

White (1984) showed a significant impairment in verbal short-term memory, and Paced auditory serial addition test (PASAT), while performance in tests like trail-making, letter-digit code, dual-task cancellation, and subtraction were unaffected by hypoxia at 3,600 m (≈13.7 kPa O_2).

Regard et al (1991) found a strong relationship between performance in cognitive tasks and symptoms of AMS. Subjects who suffered from AMS within a 24-48 hours stay at 4,559 m (≈ 12.2 kPa O_2) were mildly impaired in short-term memory (verbal learning) within 6 h after arrival at altitude. Subjects who remained healthy had a better short term memory, while subjects who developed AMS had an increased error rate in the Stroop test. However, these subjects showed an improved performance in concept identification (Regard et al, 1991).

2.2.4.3 Normobaric hypoxia

Shukitt et al (1988) reported on cognitive performance and MOOD states during a 15 days long normobaric exposure to oxygen levels of 21, 17, and 13 % O_2, (three days at each level). In a test on computer interaction, impaired performance was observed in 13 % O_2. However in tests on addition and number comparison performance was actually improved in 13 %, and in 17 % O_2. Performance on coding, number comparison, and pattern comparison tests was also improved. Subjects reported significantly higher scores in MOOD states on the sleepiness and dizziness factors the first day in 13 %.

Schlichting, Knight, and Cymerman (1988) from the same exposure concluded that transient effects of normobaric hypoxia on fine motor control dissipated rapidly at P_{O_2} of 17 kPa. They also suggest that disturbances in fine motor controls might be more prolonged at lower P_{O_2} and that motor functions such as finger dexterity and arm-hand steadiness might be more sensitive to hypoxia than cognitive tests.

From the same study Knight et al (1990) concluded that "submarine atmosphere with 17 kPa O_2 is an acceptable level but more experiments must be carried out to determine man´s symptomatic and physiologic response to living in atmospheres with 14-16 kPa O_2". Note that in this study the CO_2 level was 0.9 ± 0.2 %. High CO_2 levels counteract the effects of hypoxia on cerebral blood flow (dilatation of the blood vessels) and augment the ventilatory response to hypoxia.

Fowler et al (1987) from tests regarding serial choice reaction time estimated the threshold for performance decrements due to normobaric hypoxia to be at an arterial oxygen saturation (S_{aO_2}) of 83 %, (P_{IO_2} <15 kPa).

2.2.4.4 Summary

The available litterature does not give a clear-cut answer regarding the oxygen level at which a significant deterioration of mental performance is first seen. Acute exposures (< 1 h) appear to cause a larger decrement in mental functions than prolonged exposures, indicating that an acclimatization to hypoxia takes place (Crowley et al, 1992). Learning of a new task appears to be the most hypoxia sensitive function (Denison et al, 1966; Farmer et al, 1992). However, as mentioned above there is much uncertainty as to the level of hypoxia that will cause noticeable impairments, even during acute exposures.

3 METHODS

The purpose of this study was to accumulate further knowledge about impact of mild normobaric hypoxia on human performance, i.e. to facilitate the decision-making process regarding the use of "fire retardant atmospheres" in closed spaces.

Three normobaric confinement experiments, HYPO 1, HYPO 2, and HYPO 3 were carried out with a total of 22 men exposed to different levels of normobaric hypoxia. Figure 7 illustrates the P_{O_2} exposure profiles for the three studies.

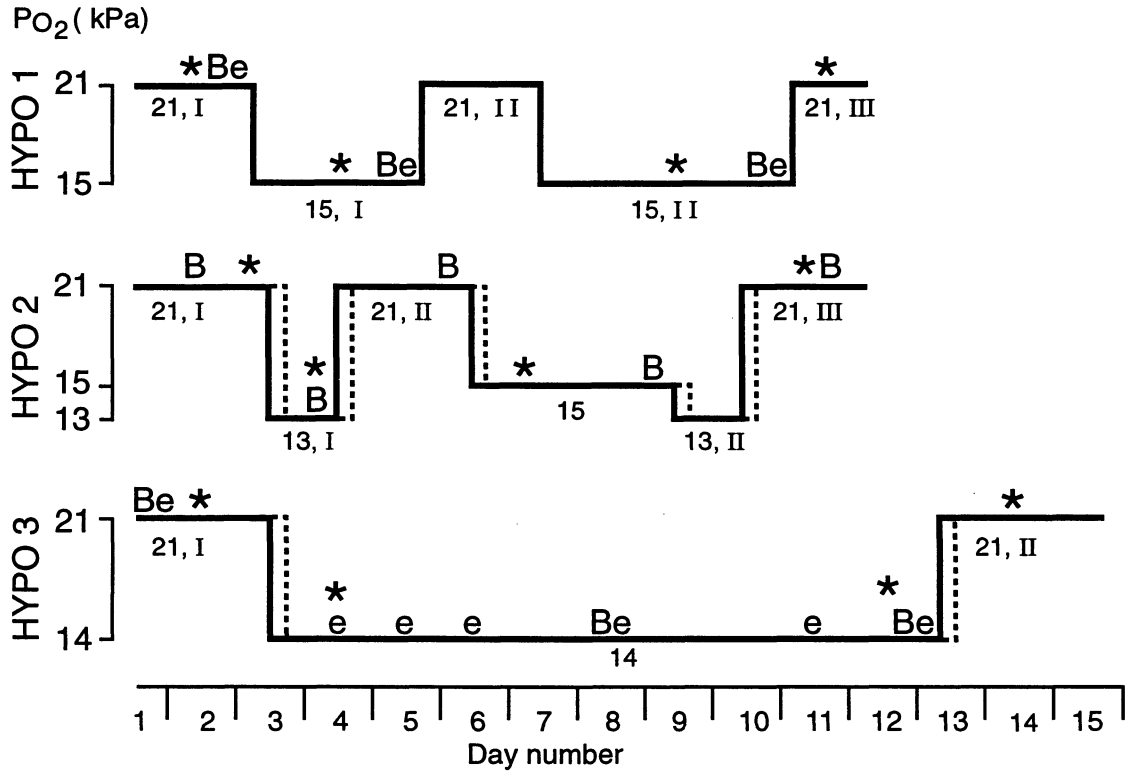


Figure 7. *Oxygen partial pressure profiles for HYPO 1, HYPO 2, and HYPO 3 (continuous lines). The broken lines indicate the 6 h delay in changed P_{O_2} level for Team B. Test occasions for Raven's advanced progressive matrices and blood sampling is indicated as follows for:*

- * *Raven's matrices*
- **e** *Blood sampling for erytropoietin analysis*
- **B** *Blood samling for other analysis*

Apart from the staff at our own department a number of scientists from different disciplines were invited to participate in the studies as listed in Table 5.

Table 5. *Participating scientists.*

	HYPO 1	HYPO 2	HYPO 3
- Sleep quality and sleep duration Mats Gillberg , Sleep Research Research Group, Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden.	X	X	X
- Cognitive tests Lena Linde, Dep. of Human Sciences, National Defence Research Establishment, Stockholm, Sweden.	X	X	X
- Swedish Performance Evaluation System, SPES Anders Ihregren, Swedish Institute for Occupational Health, Stockholm, Sweden.	X		
- Stroop test Gunilla Derefeldt, Ulf Berggrund, Dep. of Human Factors, National Defence Research Establishment, Linköping, Sweden.		X	X
- Blood analysis Bo Berglund, Dep. of Internal Medicine, Karolinska Hospital, Stockholm, Sweden.			X
- Echocardiography Mahbubul Alam, Dep. of Medicine, Section of Cardiology, South Hospital (Södersjukhuset). Stockholm, Sweden.			X
- Comprehensive Psychopathological Rating Scale (CPRS) Conny Nordin, Dep. of Psychiatry, University Hospital, Linköping, Sweden. Tove Gunnarsson, and Thomas Eklund, Dep. of Clinical Neuroscience and Family Medicine, Div. of Psychiatry, Huddinge University Hospital, Stockholm, Sweden.			X

3.1 HYPO 1

In the first study, HYPO 1, P_{O2} levels of the atmosphere was either 21 or 15 kPa. The total length of HYPO 1 was 11 days and the hypoxic periods lasted for 66 and 90 hours.

The oxygen level of 15 kPa was chosen on the basis of the results from Shukitt et al (1988) and Knight et al (1990). In their reports on flame-retardant chamber atmosphere they concluded that oxygen levels down to 17 % (approximately 17 kPa O_2) was acceptable but not 13 % (≈ 13 kPa). Regarding oxygen levels below 17 % it was also concluded that more experimental work was needed to determine man´s symptomatic and physiologic responses.

3.2 HYPO 2

The second study, HYPO 2 included hypoxic exposures to 13 kPa as well as 15 kPa O_2. The length of the experiment was 11 days. Each period with 13 kPa O_2 lasted for 24 hours and the period with 15 kPa for 72 hours. The reason for the level of 13 kPa was the somewhat conflicting results regarding what level of hypoxia that effects mental performance (see Table 3 & 4).

In HYPO 2 and HYPO 3 the change in P_{O2} was delayed 6 hours for Team B in order to allow synchronization between the change of P_{O2} and the first test period for the subjects (see figure 7). To achieve this the chamber system was separated into two isolated units with individual life support units (see Figure 8).

3.3 HYPO 3

In the third study, HYPO 3, subjects were exposed to a 10 day period with P_{O2} of 14 kPa, surrounded by shorter normoxic periods. The total length of this experiment was 14 days. As in HYPO 2 the change in P_{O2} for Team B was delayed 6 hours.

The reason for the increased duration of the hypoxia period in HYPO 3 was that in earlier experiments the time in hypoxia was thought to be too short to induce performance decrements related to hypoxia induced sleep disturbance and fatigue.

3.4 SUBJECTS

Eight subjects took part in each experiment (two subjects took part in both HYPO 1 and HYPO 2). In HYPO 3 one subject had to be removed from the chamber because of an acute upper airway infection. In all three exposures each group of eight subjects was divided into two teams (A and B). Most of the subjects were divers, submarine officers or former submarine conscripts and approved according to the medical requirements for diving and/or submarine service in the Swedish Navy. They ranged in age from 20 to 28 years. To familiarize with the facilities, tests, and environment all subject had a 2– 3 day practice period with the tests prior to the experiments.

Prior to assignment as a subject, all interested were informed both in writing and verbally about the purpose of the study, testplans, and what kind of tests they were expected to perform. They were also told that no information should be given to them regarding the composition of the atmosphere. They were all informed of their right to terminate their participation at any time during the experiment.

The project and the experimental protocols were approved by the ethical committee at the Karolinska Institute / Karolinska Hospital, Stockholm, Sweden.

3.5 FACILITIES AND ROUTINES

The tests were carried out in the hyperbaric chamber system at the Swedish Naval Diving Center (MDC), which gave a submarine like environment for the subjects.

The chamber system with facilities is illustrated in figure 8. Four parts of the chamber system which comprise a total volume of 42 m^3 were used in HYPO 1 and HYPO 2. In HYPO 3 the chamber system was extended with a tent ($\approx$ 16 m^2), a space that was used for physiological measurements and for recreation.

When off duty and when tests were completed, the subjects had access to newspapers, tv, video, and computer games. Food was locked into the chamber in connection with every watch change (every 6 hours).

The only way for the subjects to contact the outside was through the internal chamber communication system or via telephone. All windows were covered to prevent insight, decrease the influence of daylight, and to increase the feeling of isolation. The chamber operators supervised the subjects/chambers via a camera/tv system. The subjects´ contact with people from outside the chamber was limited to the medical personnel that was locked into the chamber in order to take blood samples.

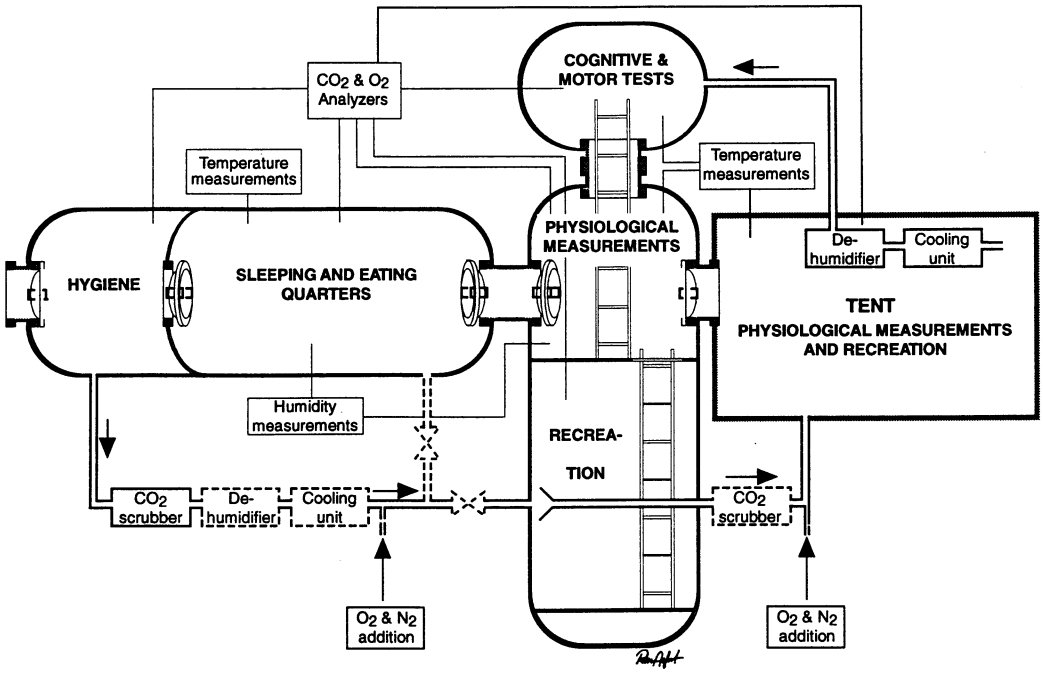


Figure 8. *Chamber system facilities at the Swedish Naval Diving Center. To be able to separate hygiene, sleeping and eating quarters from the test facilities two separate life support units were used. The supplementary life support units are marked with broken lines.*

3.6 ENVIRONMENTAL PARAMETERS

To control the environment O_2, CO_2, relative humidity and temperature were continuously registered on a paper recorder throughout the experiments. The atmospheric pressure (P_{TOT}), as measured by the meteorological station at the nearby Helicopter base, was noted every hour.

In Table 6 the average and range for the environmental parameters are listed. The chamber system commmunicated with the surrounding atmosphere and therefore followed the normal variations in atmospheric pressure. The aim was to keep P_{O2} within ± 0.2 kPa of the desired levels (21, 15, 14 or 13 kPa). CO_2-levels were not allowed to exceed limits set by the National Institute of Occupational Health: 0.5 kPa. Removal of CO_2 was effected by a life support system using soda lime. For relative humidity and temperature the goal was to keep these parameters within the same range as on board submarines, which means a relative humidity less than 70 % and a temperature between 20-30°C. A separate dehumidification circuit (SEBO 300K MT Kylprodukter, Kivik, Sweden) was connected to the life support system in order to keep temperature and humidity within the desired limits.

Table 6. Environmental parameters. Average (M) and range for the hourly readings.

	P_{O_2} (kPa)	P_{CO_2} (kPa)	P_{TOT} (kPa)	Temp. (°C)	Humidity (%)
HYPO 1					
21 kPa M	20.7	0.16	100	22	55
(Range)	(20.1-21.2)	(0.08-0.30)	(97-102)	(21-24)	(35-85)
15 kPa M	15.1	0.26	100	22	60
(Range)	(14.8-15.5)	(0.14-0.47)	(98-101)	(21-24)	(40-88)
HYPO 2					
21 kPa M	20.8	0.08	102	21	39
(Range)	(20.1-21.0)	(0.00-0.34)	(101-103)	(19-24)	(25-65)
13 kPa M	13.2	0.22	101	23	55
(Range)	(12.9-13.6)	(0.12-0.43)	(100-101)	(20-24)	(45-77)
15 kPa M	15.1	0.22	101	23	54
(Range)	(14.8-15.6)	(0.09-0.38)	(100-102)	(21-24)	(40-78)
HYPO 3					
21 kPa M	20.8	0.15	99	22	69
(Range)	(20.0-21.3)	(0.02-0.40)	(97-100)	(21-25)	(43-87)
14 kPa M	14.1	0.30	98	23	69
(Range)	(13.8-14.7)	(0.16-0.49)	(96-101)	(19-26)	(42-100)

Continuous air sampling was carried out in the chamber facility where cognitive and psychomotor tests were performed. Every hour the other chamber compartments were scanned regarding O_2 and CO_2 levels. In addition to fixed sites for gas sampling a separate long analysis line inside the chamber system made it possible to search for pockets with divergent atmosphere composition.

The P_{O_2} was measured by paramagnetic oxygen analysers (570 and 570 A, Servomex Ltd, Crowborough, Sussex, England). Carbon dioxide was measured by an infrared medical gas analyser (LB-2, Beckman, Illinois, USA). The temperature was measured with two temperature instruments (Testo 901, Testo Lenzhirch, Germany). For relative humidity measurements a humidity indicator (KM 8004, Kane-May Ltd, Great Britain) and a hair hygrometer was used.

Dilution from 21 to 15, 14 and 13 kPa O_2 was achieved through the addition of pure nitrogen (N_2) to the life support system. A reduction in P_{O_2} was effected in 10 minutes. Enrichment from 13 to 21 kPa O_2 took about 30 minutes and was accomplished by letting the dehumidifier draw air from the chamber hall instead of circulating the chamber atmosphere. The side effect of this procedure was that CO_2 and humidity levels became lower during normoxia (21 kPa) than during hypoxia. See Table 6.

3.7 STATISTICS

Variance pertaining to individual differences in level of performance was removed from the data by the following standardization of individual scores:

$$\frac{P_n}{M_{21,I}}$$

where P_n represents the level of performance at session n and $M_{21,I}$ represents mean level of performance in the first normoxic period.

Learning effects were determined using simple linear regression analysis. Since the experiments involved repeated measures on the same test, improvement due to learning is expected. Learning curves follow a power function with time or number of trials. Therefore, we performed linear regression analysis between the logarithm of standardized test scores and trial number. Such an analysis was done for normoxia and hypoxia conditions separately and also for the overall duration of the experiment. The paired *t* tests on the slope (β) and intercept (α) of each subject's regression lines were used to determine whether there were significant differences in learning rate between the conditions of normoxia and hypoxia. This analysis was also used for data from HYPO 3 although the P_{O2} exposure profile (see Figure 7), with a relatively small number of test sessions in normoxia separated by a long hypoxic period (10 days), makes this method less suitable in this case.

Analysis of variance (ANOVA) for repeated measurements was carried out to compare the overall performance of the group at different oxygen levels. To minimize confounding of hypoxia and learning effects, residuals from the overall linear regression analysis were used for the ANOVA. Test variables where paired t-tests on slope and/or intercept indicated significant differences between normoxia and hypoxia were not analysed using ANOVA.

To analyze the acute effects of changes between normoxia and hypoxia (0-12 hours), we used two–tailed paired *t* tests on the logarithm of standardized test scores. Confounding of hypoxia with learning and circadian rhythm was minimized by performing *t* tests between the mean of the two test occasions preceding and the mean of the two test occasions following a change in the P_{O2} level. For tests that were administered only once a day, paired *t* tests were carried out on the last test session before a change and the first test session following a change in the oxygen level. The Bonferroni correction for multiple *t* tests was used (Wallenstein, Zucker & Fleiss, 1980). It must be noted, however, that effects of learning are not quite separable from effects of changed oxygen partial pressure when the P_{O2} is changed from lower to higher levels if the hypothesis is that hypoxia reduces performance.

In all three exposures correlation between subjective symptoms and performance varibles was studied.

All statistical analysis was carried out using commercially available software (Stat View™ II. Abacus Concepts. Inc. Berkeley, CA). Results were regarded as significant when $p < 0.10$ ($p < 0.05$ for physiological measurements).

3.8 TESTS AND MEASUREMENTS

Twice a day the subjects completed the test battery that had been designed to measure effects of hypoxia. The watch schedule/testing procedure that is outlined in Figure 9 is the same as the one used in Swedish submarines. Each watch had 6 hours tests, 6 hours rest/sleep and so on for the whole experiment. Watch A performed their tests between 0000 and 0600 and between 1200 and 1800. The subjects in watch B had their test periods in the morning between 0600 and 1200 and between 1800 and 2400. The personnel outside the chamber had a round the clock work routine divided into 8 or 12 hour shifts.

<table>
<tr><th>Subject / Hour</th><th colspan="4">Team A</th><th colspan="4">Team B</th></tr>
<tr><th></th><th>1</th><th>2</th><th>3</th><th>4</th><th>5</th><th>6</th><th>7</th><th>8</th></tr>
<tr><td>0000</td><td>Cogn Psy. Mo</td><td>Cogn Psy. Mo</td><td>Exer</td><td>Exer</td><td colspan="2" rowspan="2">Rest / Sleep</td><td colspan="2" rowspan="2">Rest / Sleep</td></tr>
<tr><td>0600</td><td>Exer</td><td>Exer</td><td>Cogn Psy. Mo</td><td>Cogn Psy. Mo</td></tr>
<tr><td rowspan="2">1200</td><td colspan="2" rowspan="2">Rest / Sleep</td><td colspan="2" rowspan="2">Rest / Sleep</td><td>Cogn Psy. Mo</td><td>Cogn Psy. Mo</td><td>Exer</td><td>Exer</td></tr>
<tr><td>Exer</td><td>Exer</td><td>Cogn Psy. Mo</td><td>Cogn Psy. Mo</td></tr>
<tr><td rowspan="2">1800</td><td>Cogn Psy. Mo</td><td>Cogn Psy. Mo</td><td>Exer</td><td>Exer</td><td colspan="2" rowspan="2">Rest / Sleep</td><td colspan="2" rowspan="2">Rest / Sleep</td></tr>
<tr><td>Exer</td><td>Exer</td><td>Cogn Psy. Mo</td><td>Cogn Psy. Mo</td></tr>
<tr><td rowspan="2">2400</td><td colspan="2" rowspan="2">Rest / Sleep</td><td colspan="2" rowspan="2">Rest / Sleep</td><td>Cogn Psy. Mo</td><td>Cogn Psy. Mo</td><td>Exer</td><td>Exer</td></tr>
<tr><td>Exer</td><td>Exer</td><td>Cogn Psy. Mo</td><td>Cogn Psy. Mo</td></tr>
</table>

Figure 9. *The 24-h watch schedule/testing procedure used in HYPO 1 and HYPO 2. In HYPO 3 cognitive (Cogn) and exercise tests (Exer) were carried out only during the day shifts (0600 to 1800) while some of the psychomotor and motor tests (Psy. Mo) were administered during both day and night shifts. Redrawn from Linde et al, 1997. © Lawrence Erlbaum. Associates, Inc.*

	HYPO 1	HYPO 2	HYPO 3
PHYSIOLOGICAL MEASUREMENTS			
Bicycle ergometry test:			
- Arterial oxygen saturation	X	X	X
- End tidal P_{O_2}	X	X	X
- End tidal P_{CO_2}	X	X	X
- Heart rate	X	X	X
- Breathing frequence	X	X	X
- Borg estimation	X	X	X
- Tidal volume		X	X
- EKG analysis		X	X
- Oxygen uptake *			X
Echocardiography *			X
Body temperature	X	X	X
Body weight *	X	X	X
Hand grip strength		X	X
Blood analysis *	X	X	X
RAT	X		
CFF	X	X	X
COGNITIVE, PSYCHOMOTOR, AND MOTOR TESTS			
COMPUTERIZED TESTS			
Manikin		X	X
Stroop		X	X
4-Choice Reaction Time		X	X
Finger Tapping		X	X
Symbol-Coding		X	X
SPES: Swedish Performance Evaluation System			
- Symbol digit	X		
- Simple Reaction Time	X		
- Finger Tapping	X		
PAPER AND PENCIL TESTS			
Raven's Advanced Progressive Matrices *	X	X	X
Grammatical Reasoning	X	X	X
Short-Term Memory	X	X	X
PASAT	X	X	
Fine manipulative tests			
- Tracing			X
- Medium Tapping			X
- Pursuit Aiming			X
- Aiming			X
QUESTIONNAIRES			
Environmental Symptoms Questionnaire	X	X	X
Mood questionnaire	X	X	X
Sleep quality and sleep duration	X	X	X
Eysenck *		X	X
Adjectives *			X
CPRS *			X

Tests with an asterisk (*) were not carried out daily.

The number of test sessions in the chamber was 22 for each subject (HYPO 1 and HYPO 2), pretests excluded. In HYPO 3 most of the tests were carried out at daytime between 0600 and 1800 which limited the number of test sessions to 14. During night time 1800 to 0600 only self administered tests such as motor performance, and questionnaires were carried out. In order to decrease the distraction at the end of the confinements, the experiments were called of one day earlier than the subjects had anticipated. In Table 7 all the tests in the test battery are listed. Appendix A gives an example of how one six hour test battery was planned.

3.8.1 Physiological measurements

3.8.1.1 Bicycle ergometry test

Arterial oxygen saturation (S_aO_2), heart rate (HR), end tidal CO_2 (P_{ETCO_2}), end tidal O_2 (P_{ETO_2}), minute ventilation ($\dot{V}_E$), and breathing frequency (f) were measured both at rest and during standardized exercise.

Exercise were carried out on an electrically braked bicycle ergometer (Siemens Elema, Solna, Sweden). In HYPO 1 and HYPO 2 bicycle ergometry tests were carried out once every 12 hours (both during day and night shifts) and in HYPO 3 only once a day (day time). The subjects breathed through a mouthpiece connected to a one way (non-rebreathing) respiratory valve. A flow meter (Kozak turbine and compensator, K L Engineering Co, CA) was connected to the expiratory side of the breathing valve. The signal from the flow meter was integrated to yield expiratory volume. Gas was continuously sampled from the expiratory port of the breathing valve, and P_{ETCO_2} and P_{ETO_2} were measured on line (Normocap 200, DATEX, Finland). To measure the arterial oxygen saturation and heart rate a transcutaneous finger probe, was attached to the right index finger and connected to a pulse oximeter (Biox 3740, Ohmeda, Louisville, CO). All the parameters mentioned above were continuously registered on a flat bed recorder. In HYPO 3 the signals were also relayed to a microcomputer (BIOPAC Systems Inc., Goleta, CA) and stored on disc.

After the subject had been sitting at rest on the bike for 5 minutes they started pedalling at a work load of 100 Watts (W) (50 W in HYPO 3). The work periods lasted for 10 minutes. Afterwards the subjects continued to breathe through the mouthpiece for another 5 minutes. The subjects estimated their perceived maximal exertion during work according to a logarithmic scale (Borg, 1982).

Three times every test session (during HYPO 2 and HYPO 3), after 5 min at rest, after 10 min at 100 W or 50 W, and after 5 min at rest post exercise, 2 lead EKG (CM5 and modified aVF) were sampled on a solid state portable EKG recorder (Trigger, Caliber Medical Corporation Reno, NV) for later analysis of heart rate and ST changes.

In HYPO 3 the subjects were divided into two groups: training and non-training. Before and after the confinement measurements of maximum oxygen uptake ($V_{O_{2max}}$) were carried out on all subjects. For the four subjects in the training group the load corresponding to 75 % of $V_{O_{2max}}$ was calculated. In addition to the daily ergometer tests at 50 W these subjects were allowed to work at 75 % of $V_{O_{2max}}$ for 45 minutes every second day throughout the whole confinement period.

3.8.1.2 Echocardiography

Echocardiographic studies were done at the Dep. of Medicine, Section of Cardiology, South Hospital (Södersjukhuset), Stockholm before and after the confinement of HYPO 3. The subjects were examined in the left lateral recumbent position using an Aloka SSD-870 (Aloka, Deutschland GmbH, Germany) with a 2.5 MHz transducer. Different cardiac dimensions were calculated in accordance with the recommendations of the American Society of Echocardiography (Henry et al, 1980, Sahn et al, 1978). As a measure of global left ventricular systolic function the amplitude of the displacement of the atrioventricular (AV) plane towards the apex in systole was used. This parameter was recorded from the apical 4- and 2-chamber views, corresponding to the septal, lateral, anterior, and posterior walls of the left ventricle as described elsewhere (Alam & Rosenhammer, 1992). The mean value of the displacement from the above 4 sites was taken as a measure of left ventricular systolic function. Using the pulsed-Doppler echocardiography the transmitral flow velocity profiles were recorded. Left ventricular diastolic function was assessed using the ratio of transmitral early (E) and late (A) waves.

Examinations were performed during air breathing and also with subjects breathing a hypoxic gas mixture (14 % O_2 in N_2) via a mouth piece connected to a demand regulator.

3.8.1.3 Body temperature

In order to collect information on biorhythm body temperature was measured repeatedly throughout the exposures. These measurements gave an estimate of how well those subjects that were forced to change their normal working hours adapted to their new shift routine. In HYPO 1 and HYPO 2 body temperature was measured before, during, and after the cognitive and psychomotor test battery, which means every third hour and in HYPO 3 measurements were carried out every hour while the subjects were awake. In HYPO 1 only oral temperature was measured (Craftemp, Astra Meditec, Sweden). Considering the high standard deviation in oral temperature measurements (Thoren, 1988) tympanic temperature measurements were carried out in HYPO 2 and HYPO 3 (FirstTemp, Medical Market AB, Sweden). The instruments were used in a mode for rectal temperature comparissons. Oral temperatures measurements in HYPO 1 were also corrected to be compared with rectal temperature measurements (+ 0.6 °C).

3.8.1.4 Body weight

In HYPO 1 and HYPO 2 body weight of the subjects (dressed only in briefs) was measured once a day at 05.00 in the morning for watch B and at 11.00 for subjects in watch A following the main sleep periods of the subjects. An electronic bathroom

scale (Thinner, Measurement Specialities Inc, USA) was used. It had an accuracy of ± 0.2 kg and prior to the experiment it was calibrated against a precision electronic scale (TE/120 J Mettler Instrumente AG, Switzerland). In HYPO 3 body weight was measured before and after the confinement.

3.8.1.5 Hand grip strength

The maximum voluntary isometric hand grip strength (MVC) was measured twice daily. Subjects had to press a strain gauge dynamometer with extended arm (Medicinsk Apparatur, Södertälje, Sweden) three times with each hand, alternating between preferred and non-preferred hand. The dynamometer was calibrated daily prior to test periods. The dynamometer was connected to an analog instrument and to a paper recorder. The average over three trials was taken as MVC.

3.8.1.6 Blood samples.

Venous blood samples were taken three times during HYPO 1, after a day in normoxia, after 54 hours in the first hypoxia period and after 90 hours in the second hypoxia period.

In HYPO 2 blood samples were collected five times. In addition to samples taken in all three normoxia periods, samples were taken after 24 hours in the first period with 13 kPa O_2 and after 72 hours in the period with 15 kPa O_2.

In HYPO 3 the number of blood samples was increased to seven. The first samples were taken during the first normoxia period and then followed sampling after 1, 2, 3, 5, 8, and 10 days of hypoxia. All sample occasions are depicted with a "B" or an "e" in the P_{O2} profiles in Figure 7 (see chapter 3).

The blood samples were analyzed within 12 h after sampling. Analysis of erythropoietin was performed on serum that had been prepared and frozen within 5 h of sampling. In HYPO 1 and HYPO 2 blood samples were analyzed at the Dept. of Clinical Chemistry, South Hospital (Södersjukhuset), Stockholm and during HYPO 3 at the Karolinska Hospital, Stockholm, Sweden.

3.8.1.7 Glare readaptation time, RAT

Eye movements or optokinetic nystagmus (OKN) is used to measure the glare recovery time or readaptation time (RAT) after a brief exposure to a light flash. The sensitivity to light in an eye that is dazzled with a flash after beeing adapted to darkness is abruptly decreased (Wang, 1990). As a result the OKN is temporally extinguished.

Tengrot et al (1976) found that the length of the disappearance of the OKN is dependent on the oxygen partial pressure and also sensitive to alcohol, antidepressive drugs, and welding fumes (Linde,1980).

The task was to trace, and follow by eye, a light pattern (dark and light bars) projected to move from side to side on the inside of a semi sphere. Before the tests the subjects had three surface electrodes attached on the forehead and the temples to allow registration of eye movements by electronystagmografi (ENG). In order to achieve dark adaptation the subjects wore red goggles for 20 minutes before the test. The ENG signal was traced using a multi channel ink jet recorder (Mingograf 800, Siemens Elema, Sweden). The optokinetic nystagmus was used to synchronize the dazzling light flash with the eye movements of the subject, so that the flash was delivered when the subject was looking straight forward.

In each test the average adaptation time of ten dazzlings were used as raw data. In Figure 10 the experimental setup is illustrated. This test was only used in HYPO 1 because of the complexity of the test procedure and lack of time in each test session.

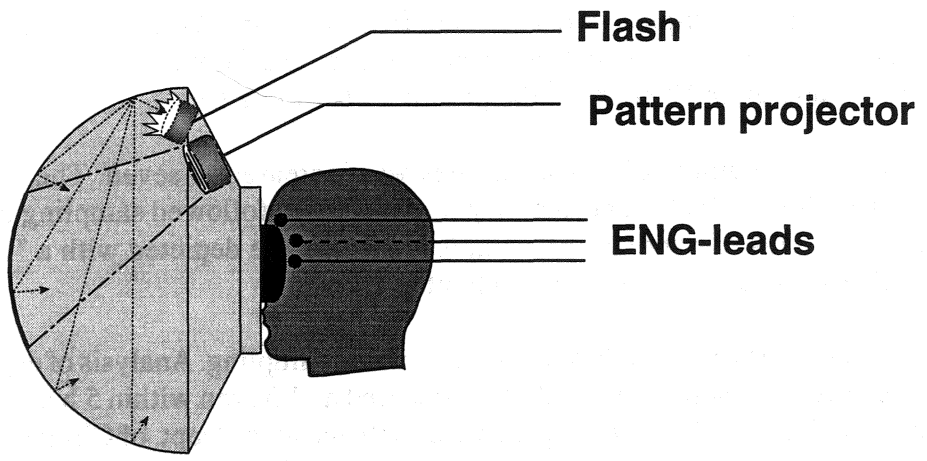


Figure 10. *Experimental setup for measurements of optical readaptation time (RAT).*

3.8.1.8 Critical flicker frequency, CFF

In the critical flicker fusion frequency test (CFF) the maximum flicker frequency at which a subject is able to discriminate between a flickering or a steady light is determined. The maximum CFF decreases as a function of central nervous system fatigue. The performance shows great inter-individual variations. The CFF test has been used in studies on drug effects on the CNS (Hindmarch, 1980), sleep deprivation (Bensimon, 1990), and as a test of objectivity in fatigue reports (Seki, 1976).

The subject placed his head in a facepiece from a radar PPI (plane position indicator) and looked into a 30 cm long 18 cm wide tube (Figure 11). Ten holes allowed a small amount of light into the tube, in the bottom of which a set of red/green light-emitting diodes (LEDs) were used as light source (backlighter HLMP 2965). The test was administered by a microcomputer Macintosh IIcx (Apple Computer Inc., Cupertino, CA) with custom made software written in LabVIEW (National Instruments, Austin, TX). The frequency interval between 25 and 45 Hz was divided into 60 frequencies which were presented to the subject in random order and color (red or green, 30 of each color). All stimuli were flickering but the subject was told to press a button when he could see the flicker. The stimulus was on for 1 s with 2 seconds dark interval between each stimuli.

The critical frequency or the frequency that subjects experienced as non flickering was identified and used as raw data for each test.

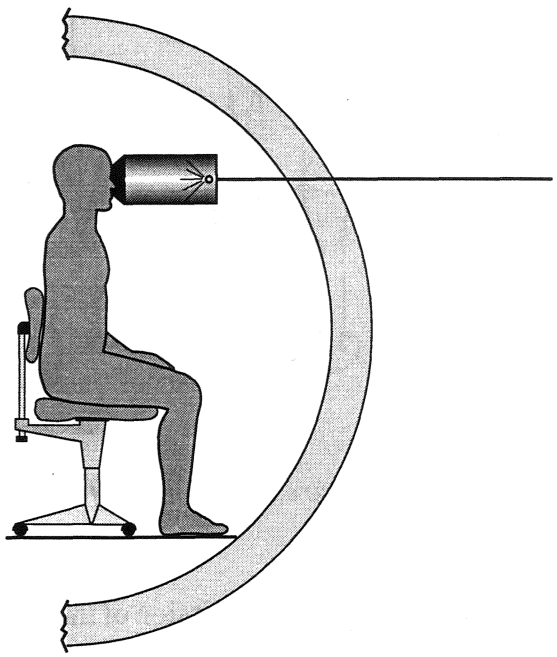


Figure 11. *Experimental setup for measurements of critical flicker fusion frequency (CFF).*

3.8.2 Cognitive, psychomotor, and motor tests

3.8.2.1 Computerized tests.

The computerized tests Manikin, 4–choice reaction time (RT), Tapping, Symbol Coding, and Stroop were all administered using a Macintosh IIcx (Apple Computer Inc., Cupertino, CA). The software for Manikin, RT, Tapping, and Symbol Coding was written in LabVIEW (National Instruments, Austin, TX) by our own staff. The Stroop programme employed a software SuperCard (Allegiant Technologies Inc. San Diego, CA).

Manikin

Manikin is a test of spatial orientation and spatial transformation. The test is designed to measure the ability to mentally manipulate objects and determine the orientation of a given stimulus. This test was originally designed to assess the ability of pilots to orient themselves with respect to an external visual reference system. The Manikin test is considered to be sensitive to relatively mild degrees of hypoxia (Crowley et al, 1992, Denison et al, 1966, Farmer et al, 1991).

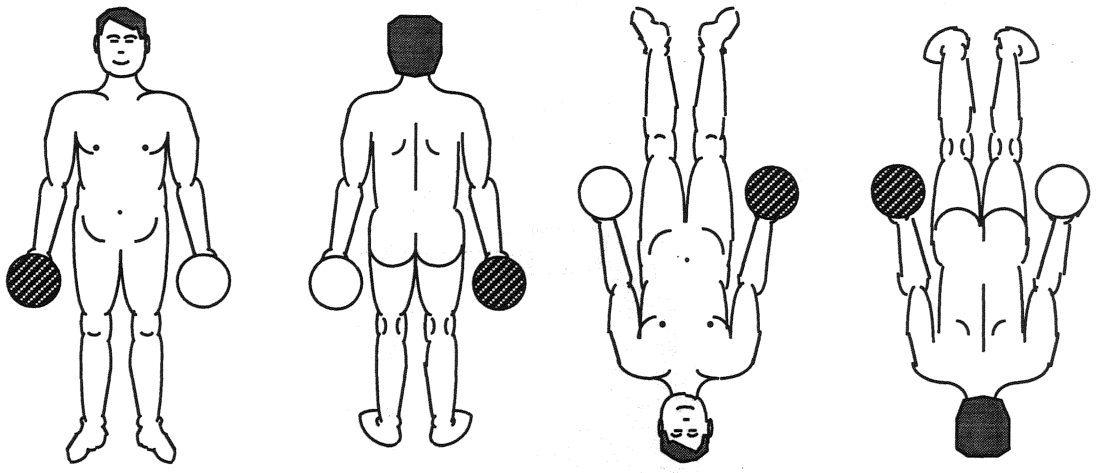


Figure 12. *The manikin figure shown in the four different orientations.*

The test used here was a computerized version of the test used by Denison et al in 1966. The task was to indicate in which hand a human figure, displayed on a computer screen, held a disc of a given color. In the test a colored rectangle (blue or orange) was first shown to the subject for 2 s, and after a 1 s pause the manikin was shown in one

of four orientations (see Figure 12). The manikin was holding a colored disc in each hand. The subjects then indicated whether the previously shown color was held in the manikin´s left or right hand by moving a joystick to the left or right. Response time was measured from display of the manikin to the moment the joystick reached its end position.

In HYPO 2 each of the 16 different combinations was presented once in each test session. In HYPO 3, each combination was presented twice. Response times and errors were recorded by the computer. In HYPO 3 results was recorded as mean, standard deviation and error rate for each of the four positions, while in HYPO 2 the positions were not separated.

Stroop color word task

The Stroop test has been used since the thirties to diagnose brain injuries (Mac Leod, 1984). The test has also been used in cognitive performance assessment batteries sensitive for performance decrements due to the use of medical drugs (Englund et al, 1987) and to study mental ability at high terrestrial altitude (Crowley et al, 1992). Stroop measures the capacity for parallel processing of relevant and irrelevant information and shows effects of interference and response competition (Englund et al, 1987).

On the computer screen 40 words (4 rows of 10 words) were simultaneously displayed in colored letters or in black letters on a grey background. These words were displayed under three different conditions:

i) words and colors were congruent, i.e. the four words `red´, `green´, `blue´, and `yellow´ were displayed in the colors red, green, blue, and yellow, respectively;

ii) words and colors were in conflict, i.e. the words for the colors were displayed in incongruent colors (e.g. the word `red´ was displayed in a green, blue, or yellow color);

iii) a control condition with the words displayed in black (word reading task); and a control condition with the letters `XXXX´ substituted for the forty words and displayed in the four colors (color naming task).

Working as quickly as possible subjects were required either to read the words aloud or to name the colors aloud. Reading time for each of the 24 screens was recorded, and means and standard deviations were computed for the different conditions.

Four choice reaction time (RT)
According to Englund et al (1987) the four choice reaction time is particularly sensitive to sleep-loss effects and has been used in studies regarding hypoxia effects (Paul & Fraser, 1994).

Four light–emitting diodes (LEDs), placed in the four cardinal directions, were lit one at a time in random order. The subject´s task was to move a joystick towards the lit LED as quickly as possible. The time interval between trials was varied randomly between 0.2 and 0.8 s. A total of 200 responses were tested in each run. The reaction time was measured as the time interval from onset of the LED until the joystick stopped at its end position. Reaction time and errors were recorded by the computer.

Tapping
Finger tapping measures the maximum rate of voluntary repetitive movement. This finger tapping task is similar to, but not the same as, the one used in HYPO 1 (see Appendix B," Swedish Performance Evaluation System" by Iregren).

The subject tapped a key as rapidly as possible with an index finger. The number of taps was counted during 5 s. Each 5 s trial was followed by approximately 15 s of rest; then the test was repeated with the opposite hand. In HYPO 2, there were 8 such trials alternating between the preferred and non-preferred hand. In HYPO 3 the number of trials was extended to 20. The number of taps and the standard deviation for both preferred and non preferred hand were recorded by the computer (see also chapter 3.8.2.2).

Symbol coding test
This test was a computerized version of a paper–and–pencil task used previously to investigate the effects of caffeine during a vigil or in the afternoon after normal sleep (Linde, 1995).

The symbol coding task is illustrated in Figure 13. The task was to translate symbols shown in the lower right part of Figure 13 into letters using a code such as the one shown in the left part of the figure and to decide if the rule shown in the upper right part was fulfilled or not. The subject answered by moving a joystick. (For details see Linde, 1995)

The items in the symbol coding task were divided into four categories: simple rule (eg. `all with B´) with one or two distinctive features and a complex rule (eg. `All A with C and B with D´) with one or two distinctive features for both letter pairs. There were 80 items with the same rule in one block. The subject was instructed to complete as many items as possible without making any errors. The test lasted for 4 blocks (320 items) or 8 minutes, whichever occurred first. Two performance variables were

analyzed: reaction time (RT) for correctly solved items and accuracy, that is, number of correctly solved items divided by the total number of items attempted.

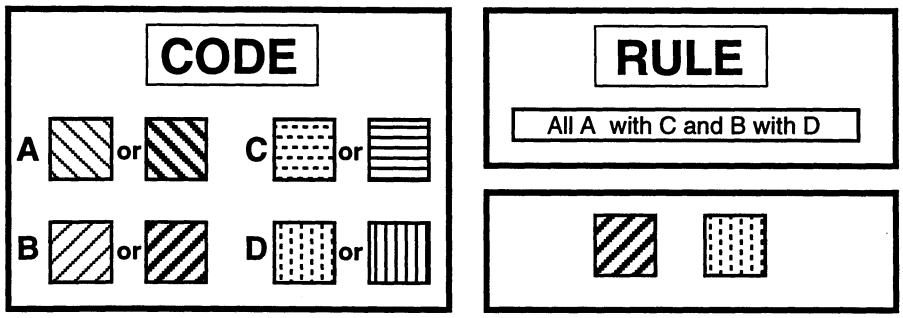


Figure 13. The symbol coding task as seen on a computer screen by the subject. On the left is an example of a code, and on the right is an example with a complex rule. Below the rule is an example of a task. A joystick was used for the responses.

Swedish performance evaluation system (SPES)

A computerized system, the Swedish Performance Evaluation System (SPES) has been developed at the Swedish National Institute for Occupational Health to assess functional changes in the central nervous system induced by exposure to unfavorable work environmental conditions (Gamberale, Iregren, & Kjellberg, 1990). From the SPES test battery the following cognitive and psychomotor tests were used: Symbol Digit, Simple Reaction Time, and Finger Tapping. The test battery was administered by a portable computer (Toshiba 3200) connected to a printer outside the chamber. For more iformation see Appendix B," Swedish Performance Evaluation System", by Iregren.

3.8.2.2 PAPER AND PENCIL AND AUDITIVE TESTS

Raven´s Advanced Progressive Matrices

Raven´s advanced progressive matrices is considered to measure general intellectual ability and involves inductive reasoning on the basis of nonverbal information (Raven, Court, & Raven, 1983). The complete advanced version comprises 36 items. Using results from prior studies (Linde, 1995; Linde & Bergström, 1992) 4 parallel and equally difficult versions were composed. Each 10-min version comprised 9 items. Raven´s advanced progressive matrices was only presented four times during each experiment. In Figure 7 (see chapter 3) those occasions are indicated by an asterisk (*).

Grammatical Reasoning

The grammatical reasoning test involves the understanding of printed sentences of various levels of syntactic complexity. Performance on the test has been shown to be sensitive to a number of stressors (Baddeley, 1968) and has also been used in relation to hypoxia (Green & Morgan, 1985).

The task is basically to decide whether sentences such as "A precedes B" are true descriptions of figures, for example "A B" (Baddeley, 1968). In this study the subjects were asked to indicate the correctness of items presented in the form:

A precedes B *A B* *True*

that is, to determine the correctness of the statement *false* or *true* given in the item and mark the correct answer. Sentences can be presented in affirmative or negative, and in passive or active mode. Subjects were given 3 min to complete as many as possible of 64 items. A paper-and-pencil version was used. To reduce the number of dependent variables, level of performance was defined as:

$$\text{Efficiency}=\left(\frac{\text{no. of correct items}}{\text{no. of solved items}}+\frac{\text{no. of solved items}}{64}\right)\cdot\frac{1}{2}$$

A subject who solved all 64 items correctly would score 1.0.

Short-Term Memory, (STM)

Tests of short term memory have been used in order to detect the effect of hypoxia on mental ability (Crow & Kelman, 1971; Regard et al, 1991).

Series of 10 random numbers between 0 and 99 were presented to the subject through headphones from a pre-recorded tape. The subject´s task was to write down as many numbers as possible, in free order, immediately after the presentation of a 10-number series. Each test session consisted of five series, which took about 5 min. The series used at a given test session were chosen from a pool of 50 series. The average number of correctly recalled items over five lists of numbers was used as raw data for each subject.

Paced Auditory Serial-Addition Test (PASAT)

PASAT is a mental arithmetic test which measures the rate of information processing. The test is used clinically to estimate individual performance during recovery from concussion (Gronwall & Wrightson, 1974; Gronvall, 1977). PASAT has also been used to measure narcosis during hydrogen breathing at elevated pressure (Adofsson, Örnhagen, & Ingvar, 1984) as well as effects of hypoxia (White, 1984).

Subjects were presented a single digit (2 to 9) every other second through headphones from a pre-recorded tape. There were 10 tapes, with series of random digits. The task was to swiftly add the two numbers last given and reply verbally, thus the second digit was added to the first, the third to the second and so on. In HYPO 1 a total of 70 digits were given. In HYPO 2 and HYPO 3 the number of digits was increased to 100. All the answers were recorded on tape. The total number of correctly performed additions was noted.

Fine manipulative tests

Because finger tapping performance appeared to improve under hypoxia in HYPO 2, four additional tests of motor skills (Fleisman & Ellison, 1965) were included in HYPO 3. These fine manipulative tests measures wrist-finger speed emphasizing rapid pendular and/or rotary wrist movement, and aiming or the ability to perform quickly and precisely a series of movements requiring eye-hand coordination. The tests are illustrated in Figure 14.

Tracing. The subject was required to trace the path through a maze pattern without allowing the pencil to touch any of the maze lines. The number of openings correctly marked within 50 s and the number of errors/total number of traced openings were scored.

Medium Tapping. The subject made three dots in each of a series of circles (diameter 10 mm), taking the circles in any order he wished. Dots placed outside of circles were counted as errors. The number of correctly completed circles in 30 s and the number of errors/number of circles attempted were scored.

Pursuit Aiming. In this test the subject followed a pattern of small circles (diameter 5 mm), placing a dot inside each circle. Dots placed outside of circles were counted as errors. The number of dots placed correctly in 30 s and the number of errors/ total number of circles attempted were scored.

Aiming. The subject placed one dot in each of a series of small circles (diameter 3 mm) Dots placed outside of circles were counted as errors. The number of dots placed correctly in 60 s and the number of errors/total number of circles attempted were scored.

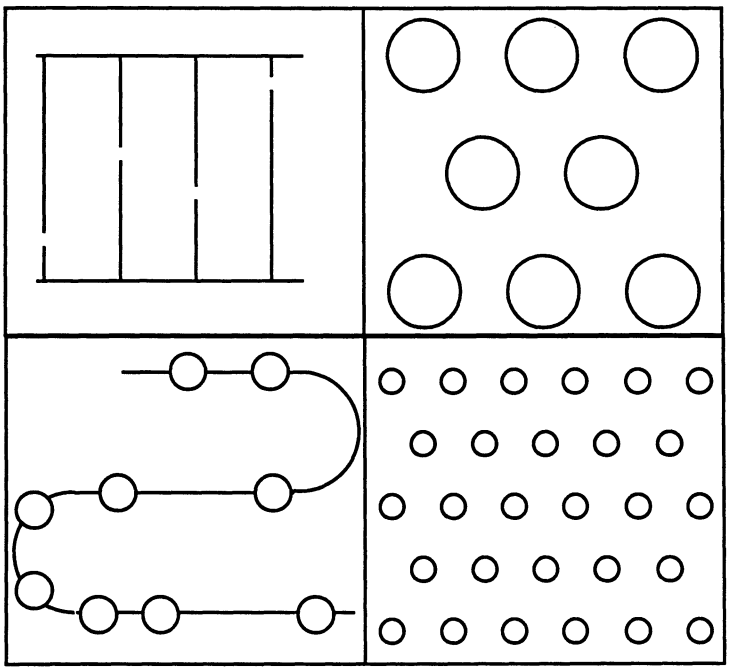


Figure 14. *Full-scale cuts from the paper-and-pencil tests Tracing, Medium Tapping, Pursuit Aiming, and Aiming.*

3.8.3 Questionnaires and subjective data

3.8.3.1 Environmental Symptoms Questionnaire (ESQ)

The Environmental Symptoms Questionnaire (ESQ III) has been validated in studies of AMS (Crowley et al, 1992; Regard et al, 1991; Sampson et al, 1983). The questionnaire contains 67 questions concerning respiratory symptoms, central nervous system problems, symptoms from ear, nose, and throat, fatigue, and alertness. Symptom ratings are made on six point scales with verbal labels, ranging from 0, labelled "Not at all" to 5, labelled "Extreme". Symptoms of mountain sickness are normally associated with scores above 0.6 for respiratory (AMS-R) and 0.7 for cerebral symptoms (AMS-C).

The subjects filled in the questionnaire on 2 occasions prior to the confinement. In HYPO 1 the questionnaire was a part of the SPES-test battery which was administered by a microcomputer (Toshiba 3200). In HYPO 2 and HYPO 3 a paper and pencil version was used.

3.8.3.2 Self rating of mood

Mood scales have been used earlier in studies regarding hypoxia (Crowley et al, 1992; Shukitt et al, 1988). The mood adjective check list used here has been constructed in order to describe mood during work and consists of a score that is computed in two mood dimensions, activity and stress, as identified by factor analysis (Kjellberg & Iwanowski, 1989).

The scale consists of 12 mood descriptive adjectives coupled to a six category response scale. The response categories have verbal labels ranging from "not at all" to "very much". The scales are bipolar with three adjectives representing each pole. Ratings are given by typing the number of the appropriate response alternative. The score in each scale is computed as a mean of the ratings of the six adjectives after a reversal of the response scale for the lower pole items.

In HYPO 1 the Mood scale was a part of the SPES-test battery which was administered by a microcomputer (Toshiba 3200). In HYPO 2 and HYPO 3 a paper and pencil version was used.

In HYPO 3 a more extended version of the MOOD scale was added to the test protocol on the first day of hypoxia (Sjöberg, Svenssson, & Persson, 1979). The questionnaire consisted of 71 mood descriptive adjectives coupled to a four category response scale. The different adjectives were bipolar and computed in six dimensions. Pleasantness, activation, and tension are considered basic mood dimensions while social orientation, social interaction motive, and control are related to the subjects social situation.

3.8.3.3 Self rating of sleep and alertness

After each sleep period the subjects filled in questionnaires regarding duration of sleep period, quality of sleep. In HYPO 1 and HYPO 2 alertness was rated every other hour during the test periods. In HYPO 3 this rating was carried out every hour during test periods. For more information see Appendix F, "Sleep duration, subjective sleep quality and sleepiness/alertness" by Mats Gillberg

3.8.3.4 Personality dimensions

It was speculated that personality dimensions might be affected by long time confinement, therefore two different personality inventory forms were used; Eysenck and Adjectives.

Eysenck
The personality dimention extra/introversion was estimated using the Eysenck Personality Inventory (EPI), form B (Eysenck & Eysenck, 1964). This test was administered in all three exposures. In HYPO 1 and HYPO 2 the inventory was presented in connection with the confinement and in HYPO 3 it was presented during the pre exposure training and after 12 days in confinement. The scale is constructed in such a way that high scores imply high extraversion.

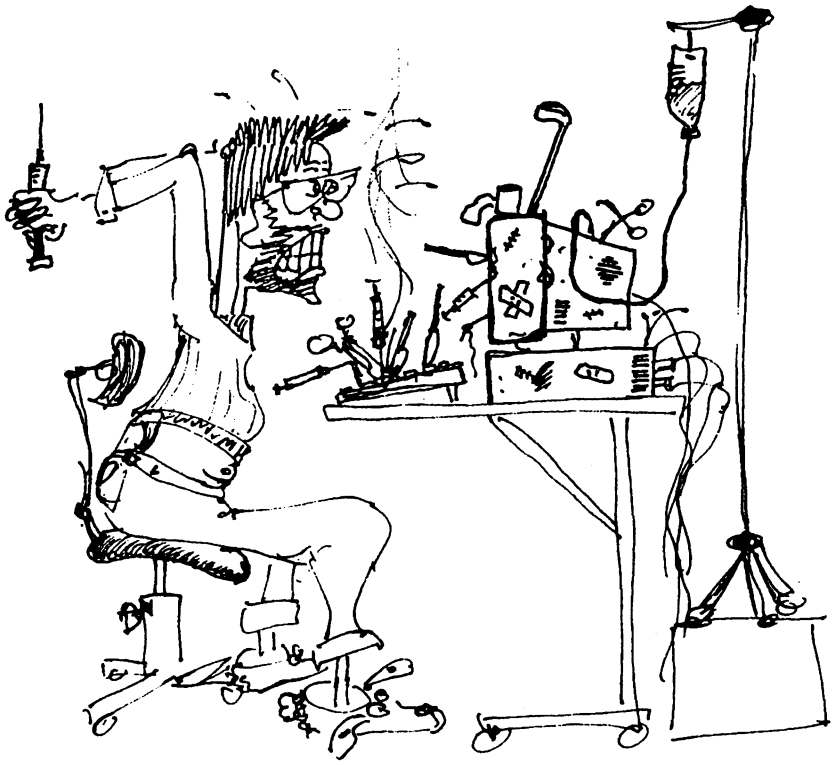
Adjectives
The five personality dimensions extraversion/introversion, agreeableness, conscientiousness, neuroticism/emotional stability, and intellect (Big Five) established by Goldberg, (1981) was measured using a questionnaire with 48 adjectives.

The adjective list that has been used (Carlstedt, 1995) was a modified version of the adjective list published by De Raad in 1992. The list of 48 adjectives that was presented to the subjects on two occasions: during the pre-exposure training and after 12 days in confinement (last day in hypoxia). The adjectives coupled to a seven category response scale from 1 labelled "no accordance at all/do not agree" to 7 "completely in accordance/totally agree". Mean and standard deviation for the five personality dimensions were calculated.

Comprehensive psychopathological rating scale (CPRS)

The CPRS was initially constructed as an instrument to evaluate changes in psychiatric disorders with treatment (Åsberg et al, 1978). It was speculated that in the wide range of psychopathological variables covered by the CPRS effects from confinement could be detected.

Ratings were performed by psychiatrists on three different occasions; before, after 6 to 9 days in confinement, and after confinement. For more information see Appendix G, "Psychiatric ratings of volunteers during stay in a pressure chamber" by Thomas Eklund, Tove Gunnarsson, and Conny Nordin.



REASON FOR INCOMPATIBILITY BETWEEN COMPUTER AND RESEARCHER

Cartoon made by one of the subjects in HYPO 2

4 RESULTS

4.1 PHYSIOLOGICAL RESULTS

4.1.1 Bicycle ergometry test

In Table 8, Figure 15 and Appendix B are shown results from the physiological measurements during bicycle ergometry at different P_{O_2}. Note that the resting values are collected with the subject sitting on the bike for 5 minutes immediately before the subject starts pedalling.

Table 8. *Physiological parameters measured during the first normoxic period and during the first day of the first exposure to different levels of hypoxic gas mixtures.*

P_{O_2}, period	21 kPa, I			15 kPa, I		14 kPa, I		13 kPa, I	
Work load (W)	Rest	100	50	Rest	100	Rest	50	Rest	100
HYPO #	1,2,3	1, 2	3	1	1	3	3	2	2
Number of subjects (*n*)	23	16	7	8	8	7	7	8	8
Sa_{O_2}, %	96	96	96	92 *	88 *	91 *	88 *	90 *	78 *
Pulse rate , BPM	85	120	102	87 *	124*	95	105	94 *	140*
End tidal O_2, kPa	13.7	14.3	14.7	9.8 *	9.4*	8.5 *	8.5*	9.6*	9.1 *
End tidal CO_2, kPa	5.1	6.5	4.8	5.0	5.6*	4.9 *	5.5*	4.5*	5.4 *
Breaths per minute	14	17	13	16	19	11	12	17	20
Ventilation, l/min	9[1]	29	20	11 [2]	36[2]*	11 *	24 *	11	38 *

[1] Data from HYPO 2 & 3 (n=15)
[2] Data from HYPO 2
n number of subjects
* significantly different from measurements at 21 kPa O_2, I ($p < 0.05$).
For better understanding see P_{O_2} exposure profiles in figure 7.

As expected arterial oxygen saturation (Sa_{O_2}), end tidal P_{O_2}, and end tidal P_{CO_2} both at rest and during exercise showed significantly lower values in the first exposure to each hypoxic level 15 kPa (HYPO 1), 14 kPa (HYPO 3), and 13 kPa O_2 (HYPO 2) compared to their respective mean levels in the first normoxic period. Pulse rate at rest and during 100 Watts (W) exercise in both 15 and 13 kPa O_2 was significantly higher than normoxic values ($p < 0.05$).

In HYPO 3, during breathing of 14 kPa O_2 the increase in pulse rate was not statistically significant neither during rest nor during exercise. It shall be noted that the number of subjects was only 7 in HYPO 3 (compared to 8 in each for the previous studies) and the load was only 50 W compared to 100 W in HYPO 1 and HYPO 2. These differences between the studies can partly explain the lack of statistical significant difference for HR in 14 kPa O_2. In Figure16 heart rate is plotted against S_{aO_2} and P_{IO_2} during rest and during exercice.

Increased minute ventilation was observed at all hypoxic levels during work compared to normoxia, while during rest the increase was not statistically significant for exposure to 13 kPa O_2. Breathing frequency did not show any significant differences between normoxia and hypoxia. Perceived exertion was graded somewhat higher during hypoxia but it was only the 15 kPa O_2 level in HYPO 1 that showed significantly increased ratings on the BORG scale.

A significant increase in breathing frequency with time was seen during prolonged hypoxic exposures. A decrease in P_{CO_2} and a significant increase in S_{aO_2}, especially during exercise, was also seen with time in hypoxia (Figure 15). Comparison between the first and last normoxic control periods showed that breathing frequency was increased by 2-3 breaths/min and end-tidal P_{CO_2} was decreased by 10-15 % (0.4-0.6 kPa) by the end of the confinement (Figure 15).

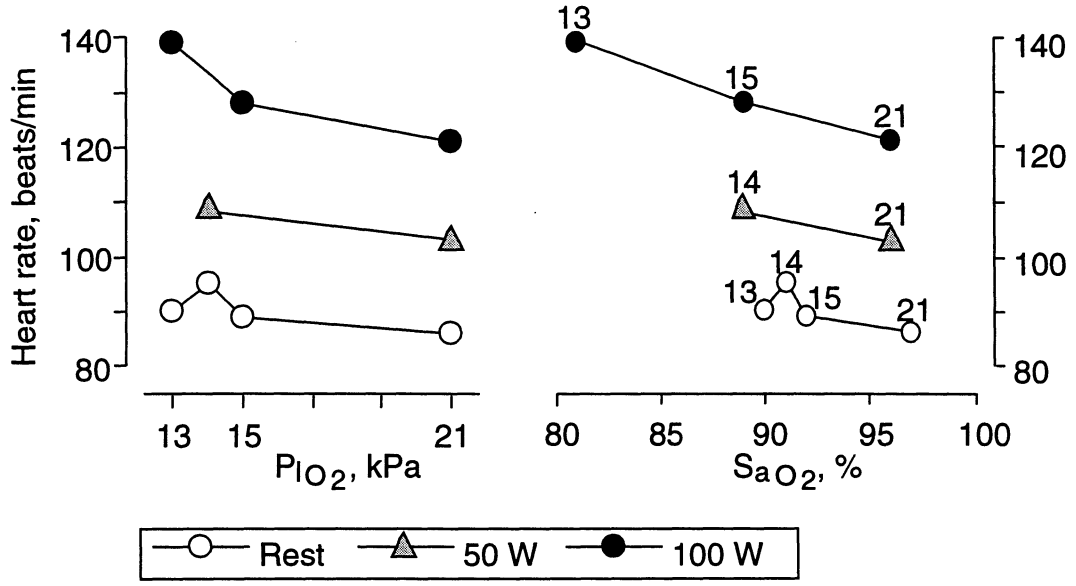
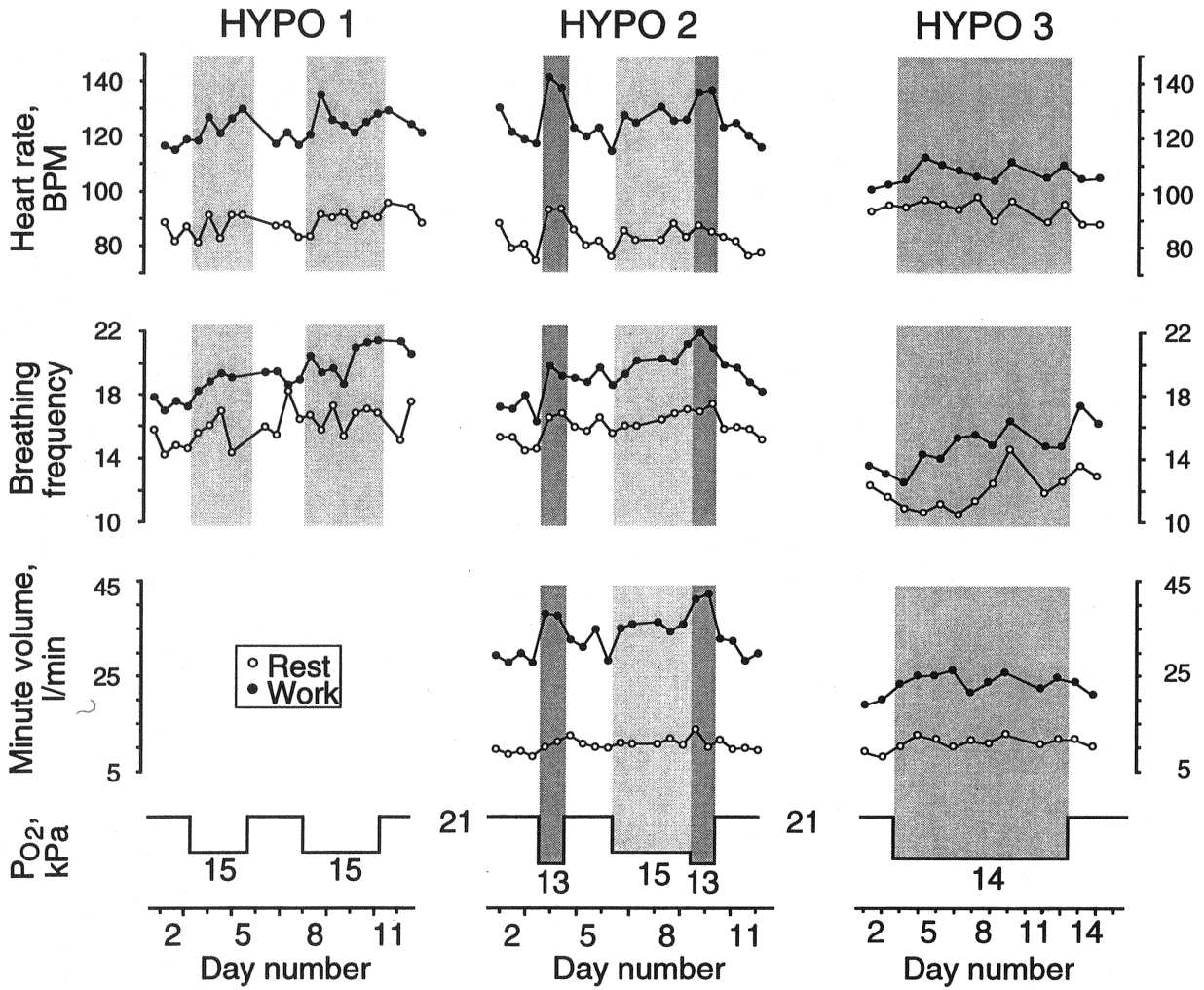


Figure 16. *Heart rate (HR) is plotted against S_{aO_2} and P_{IO_2} during rest and during exercice.*


HYPO 1
HYPO 2
HYPO 3
Heart rate, BPM
140
120
100
80
Breathing frequency
22
18
14
10
Minute volume, l/min
45
25
5
Rest
Work
P_{O_2}, kPa
21
15
15
13
15
13
21
14
2 5 8 11
2 5 8 11
2 5 8 11 14
Day number
Day number
Day number

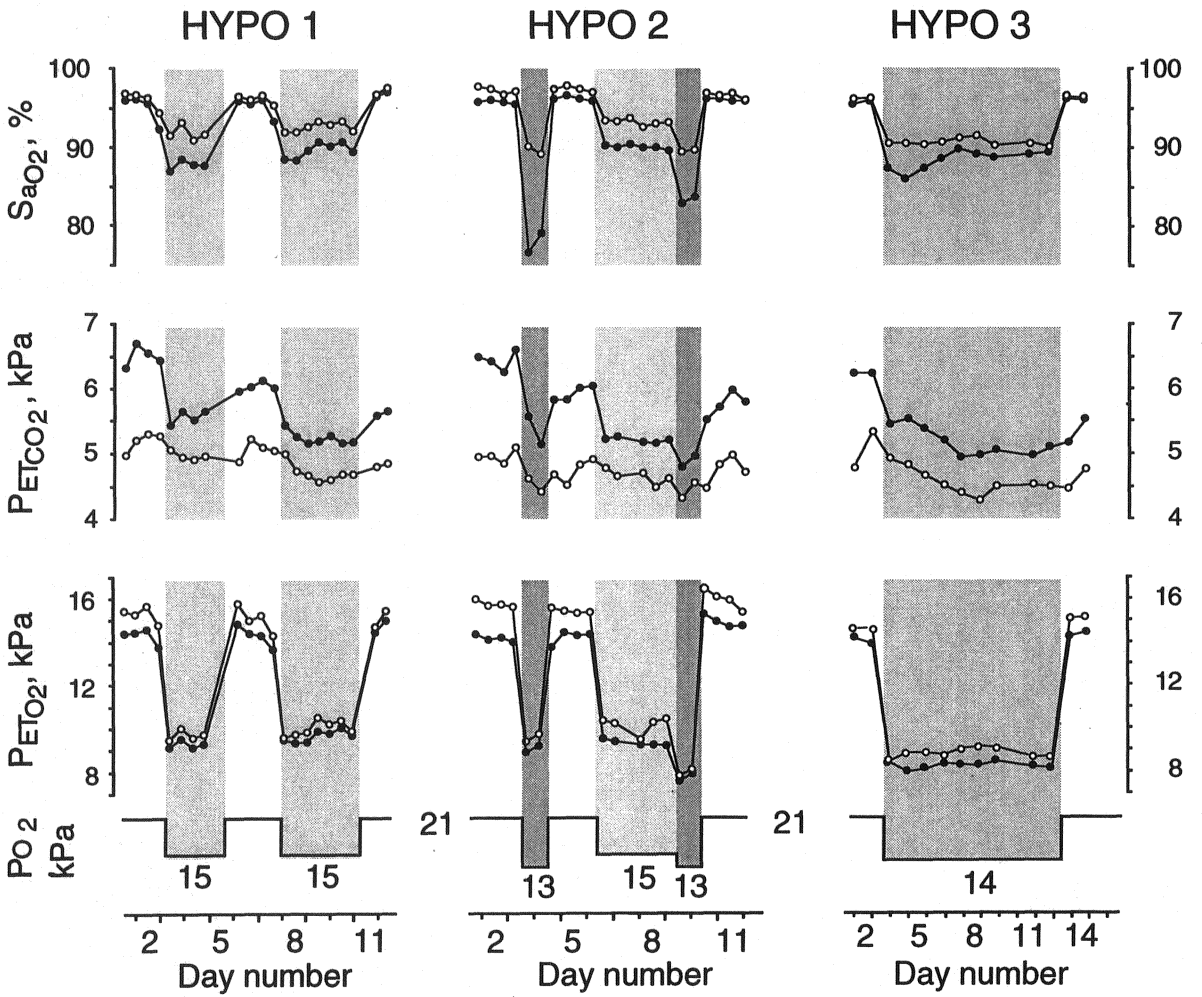


Figure 15. *Results from physiological measurements during bicycle ergometry at different oxygen levels. In HYPO 1 (n=8) and HYPO 2 (n=8) the work load was 100 and in HYPO 3 (n=7), 50 W.*

A significant correlation between end-tidal P_{CO_2} during the first control period in normoxia and during hypoxia was found during exercise at 100 W but not during exercise at 50 W or during rest. Subjects with high end-tidal P_{CO_2} concentrations during exercise in normoxia also had a higher P_{CO_2} during hypoxia. The difference in ventilation affected the arterial oxygen saturation in hypoxia (Figure 17), thus subjects with high P_{CO_2} in normoxia showed a low S_{aO_2} during the initial exposure to hypoxia. No correlation was found between oxygen saturation and ESQ scores.

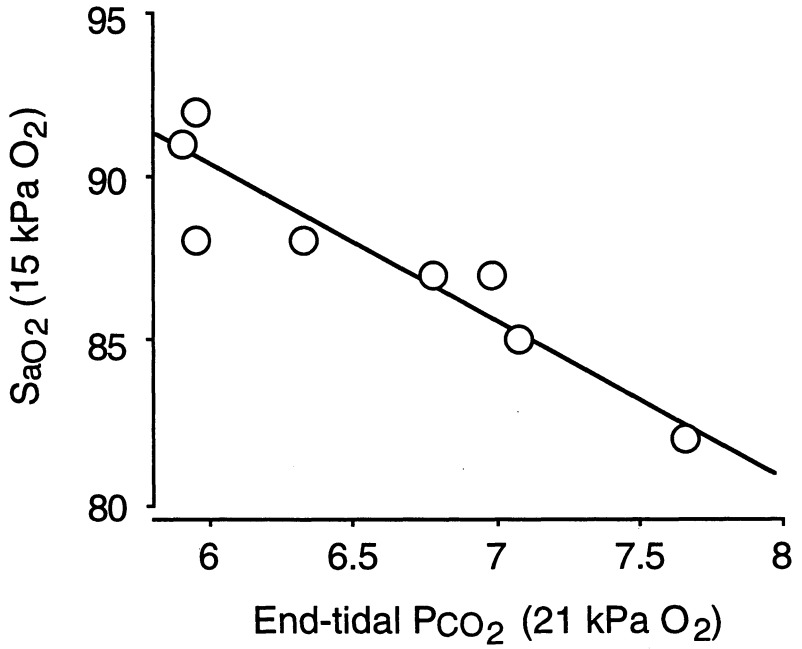


Figure 17. *Correlation between end-tidal P_{CO_2} during exercise in normoxia (control measurements in HYPO 1) and arterial oxygen saturation (S_{aO_2}) measured during first hypoxic exercise (HYPO 1, 15 kPa). n= 8.*
S_{aO_2} (%) = -4.479 P_{CO_2} + 117.0; r^2=0.841, $p<0.01$.

During HYPO 2 and HYPO 3 two-lead ekg-signals were recorded during exercise tests using a portable ekg-recorder (Trigger, Caliber Medical Corporation, Reno, NA). The system gives an automated analysis of heart rate and elevations/depressions of the ST-segment.

Apart from one subject (see below) no pathological ekg-signals appeared during the confinements. No extra-systolic beats were recorded during the exercise tests during hypoxia. No significant changes in average ST-depression or elevations during the hypoxic periods were found.

However, in one subject during HYPO 2 an increasing depression of the ST-segment with time was observed in the modified aVF lead. The depression did not appear to be related to the inspired oxygen partial pressure (Figure 18). Although, the subject did not complain of any symptoms indicating cardiac ischaemia, when the depression reached 2 mm in 15 kPa oxygen atmosphere, the subject was taken out of the chamber. An ekg recorded after the subject had been allowed to rest outside the chamber was normal, and a clinical exercise-ekg test, carried out at the department of Clinical Physiology at the University Hospital of Stockholm (Karolinska Sjukhuset) was also found to be normal. Provocation with hypoxic gas did not elicit any depression of the ST-segment. The subject was allowed to reenter the chamber after 24 hours rest. Subsequent exposure to 13 kPa O_2 for 24 hours did not produce any changes in ST-segment elevation.

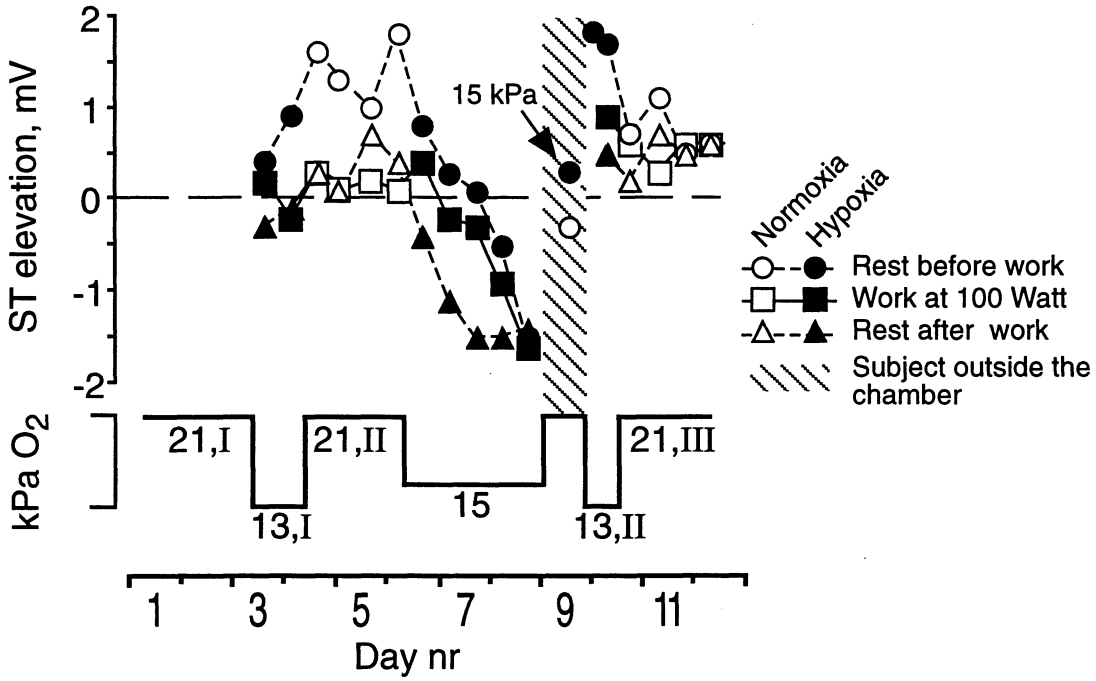


Figure 18. *Plots of ST-segment for one subject in HYPO 2*

Before the confinement started in HYPO 3 the maximum oxygen uptake was measured on bicycle ergometer. The average oxygen uptake was 43 ± 7 ml /kg with a range between 30 - 48 ml/kg. Based on the oxygen uptake test the subjects were divided into two matched groups; a training group and a control group. Unfortunately, one subject in the control group had to withdraw due to an upper airway infection. The training group exercised for 45 min every other day at 75 % of maximum oxygen uptake. None of the subjects had any problems completing the exercise during hypoxia.

No significant increase in oxygen uptake was found when maximum oxygen uptake was measured after the confinement (Figure 19), nor was there any difference between the subjects change in oxygen uptake between the training group (+2.1 % ± 4.6 %, n = 4, ns) and the control group (+7.6 % ± 5.5 %, n = 3, ns).

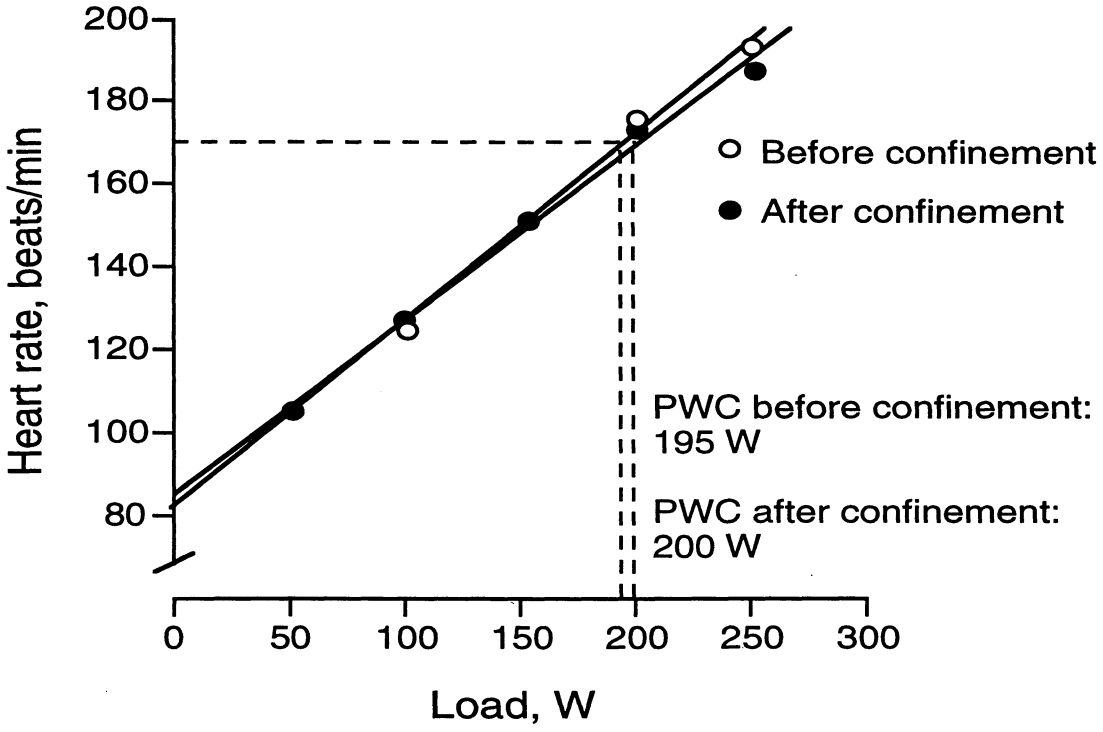


Figure 19. *Average heart rate during determination of maximum oxygen uptake before and after confinement in HYPO 3. Calculated average physical working capacity (PWC) is indicated.*

4.1.2 Echo-cardiography

During HYPO 3 an echo-cardiographic study with measurements of cardiac dimensions, AV-plane displacement and Doppler measurements of trans-mitral flow velocities was carried out to investigate if a prolonged period in hypoxia would cause any changes in cardiac activity and cardiac dimensions. An earlier report (Svedenhag et al, 1994) has shown an increased calculated left ventricular mass after 30 days training at altitude. Measurements were performed the day prior to the start of the confinement and 24 hours after the end of confinement. Measurements were carried out during air breathing and during breathing of a hypoxic gas mixture, containing 14 % O_2 in N_2, on mask. The subjects were allowed to breathe the hypoxic gas for 10 minutes before the measurements were carried out.

All results, both before and after confinement, were within the normal range. There were no significant differences between measurements in normoxia and during acute hypoxia (Table 9 and 10). No indication of any changes in cardiac dimensions nor any effects on systolic function, as assessed by the AV-plane displacement, were found to have been caused by the hypoxic confinement (Table 9).

The trans-mitral flows were also unaffected by the acute hypoxia (Table 10), but the early diastolic flow velocity (E-wave) was significantly reduced in the post-confinement measurement both during normoxia and hypoxia (Table 10). The E/A-ratio was, however, not affected neither by acute hypoxia nor by the 10 day hypoxic confinement.

4.1.3 Body temperature

In Figure 20, average body temperature during the first and second halves of the confinements, respectively, are plotted separately against time of day for Team A and Team B. Note that the adjustment in diurnal rhythm is gradual and not momentary as falsely indicated by this division in the graph. Temperature measurements in HYPO 1 was carried out with a more unreliable method (oral measurements), statistical analysis and comparison with tympanic measurements from HYPO 2 and HYPO 3 must therefore be taken with precaution.

In the first part of the confinements, both teams maintained their normal diurnal rhythm. That is, their body temperatures decreased during the night, with the lowest level reached in the early morning, and increased throughout the day.

Subjects in Team B, who kept normal sleeping habits between midnight and 0600, showed the same temperature pattern in the first and second halves of the experiments with exception for HYPO 1 where subjects more frequently slept during the afternoon rest period (1200-1800) resulting in a lowering of the body temperature in the second part of confinement over that time.

Subjects in Team A, on the other hand, tended to adjust to the change in diurnal rhythm in the second half of the confinement by lowering their body temperature to their new main sleep period (1200).

A comparison between HYPO 1-3 of temperature patterns from the first halves of the confinements shows a difference in night-time temperature for Team A. This is probably due to metabolism-increasing physiological tests carried out during the night in HYPO 1 and HYPO 2, whereas only psychomotor testing was performed between 1800 and 0600 in HYPO 3.

Table 9. *Echocardiography before and after confinement. Measurements performed during air breathing and breathing of a hypoxic gas mixture on mask (14 % O_2 in N_2). Results are means ± 1 SD.*

	Left Ventricular dimension (mm)	Left atrial dimension (mm)	AV-plane displacement (mm)	Right Ventricular dimension (mm)
Normoxia before confinement	50.7 ± 2.5	36.0 ± 4.0	15.7 ±1.5	20.3 ± 2.3
Normoxia after confinement	49.0 ± 2.5	35.0 ± 6.0	15.3 ±1.0	22.0 ± 2.4
Hypoxia before confinement	52.0 ± 3.1	34.0 ± 2.0	15.5 ±0.9	21.0 ± 2.5
Hypoxia after confinement	50.0 ± 2.0	33.5 ± 1.5	14.9 ±1.8	22.0 ± 2.9

Table 10. *Doppler cardiography before and after confinement. Measurements performed during air breathing and breathing of a hypoxic gas mixture on mask (14 % O_2 in N_2). Results are means ± 1 SD.*

	E-wave (m/s)	A-wave (m/s)	E/A-ratio
Normoxia before confinement	0.96 ± 0.08	0.59 ± 0.12	1.65 ± 0.39
Normoxia after confinement	0.74 ± 0.05 **	0.47 ± 0.09	1.62 ± 0.26
Hypoxia before confinement	0.96 ± 0.14	0.61 ± 0.12	1.57 ± 0.26
Hypoxia after confinement	0.76 ± 0.08 **	0.53 ± 0.10	1.45 ± 0.16

** $p < 0.01$ comparison with normoxia before confinement

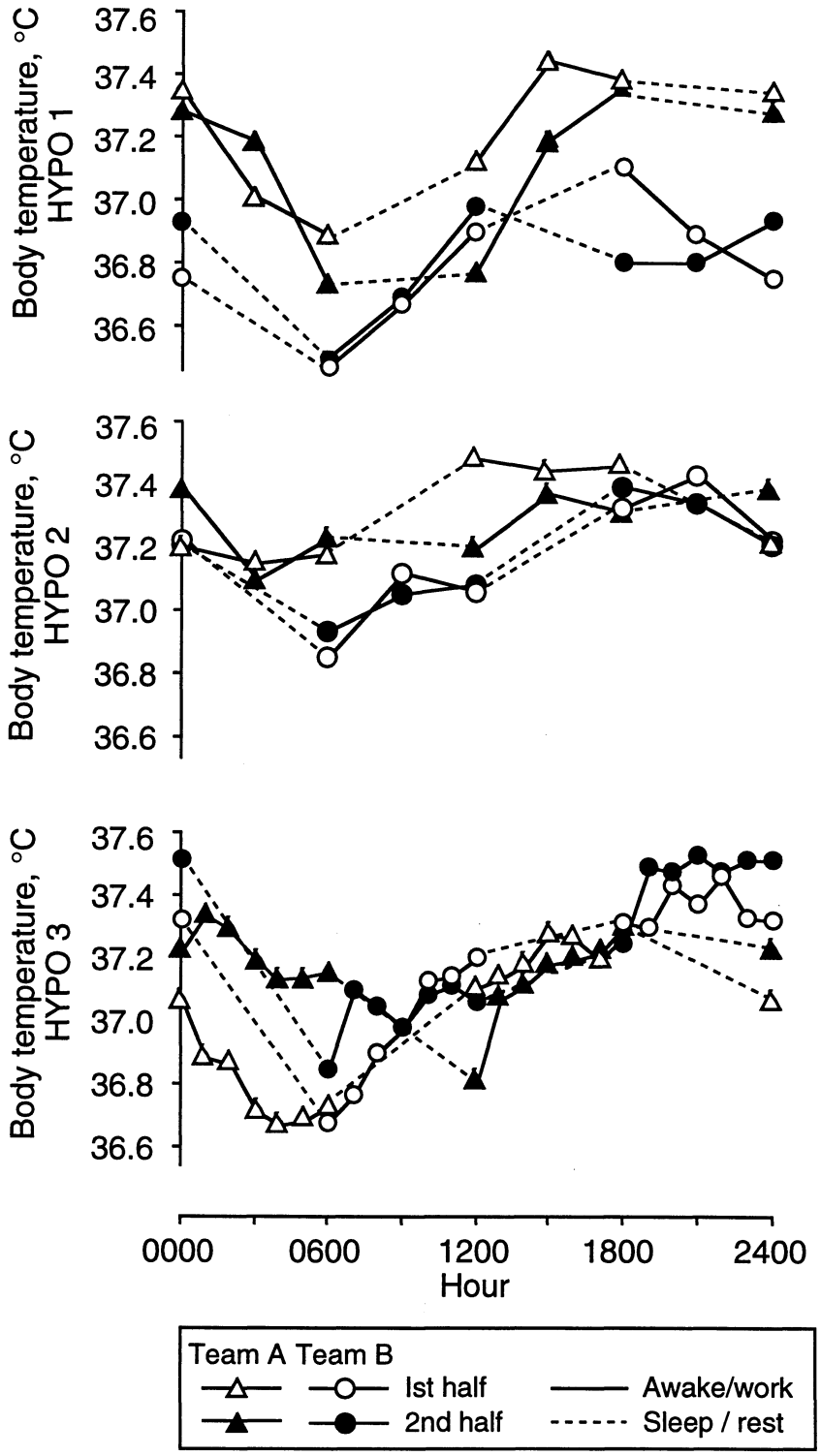


Figure 20. *Oral and tympanic measurements of body temperature. The temperatures are corrected to allow comparison with rectal measurements. The average temperature for each team of subjects during the first and second halves of the confinements are plotted against time of day.*

4.1.4 Body weight

In HYPO 1 the average weight loss was 1.2 ± 1.3 kg ($p < 0.05$) and in HYPO 3, 1.3 ± 1.3 kg ($p < 0.05$). However, in HYPO 2 the average weight showed no statistical significant change during the confinement (0.1 ± 1.2 kg).

4.1.5 Hand grip strength

Mean and standard deviation for hand grip strength at different oxygen levels are presented in Appendix B and in Figure 21. There was no significant change in relation to changed P_{O2} but in HYPO 3 linear regression indicated better performance with time for the preferred hand.

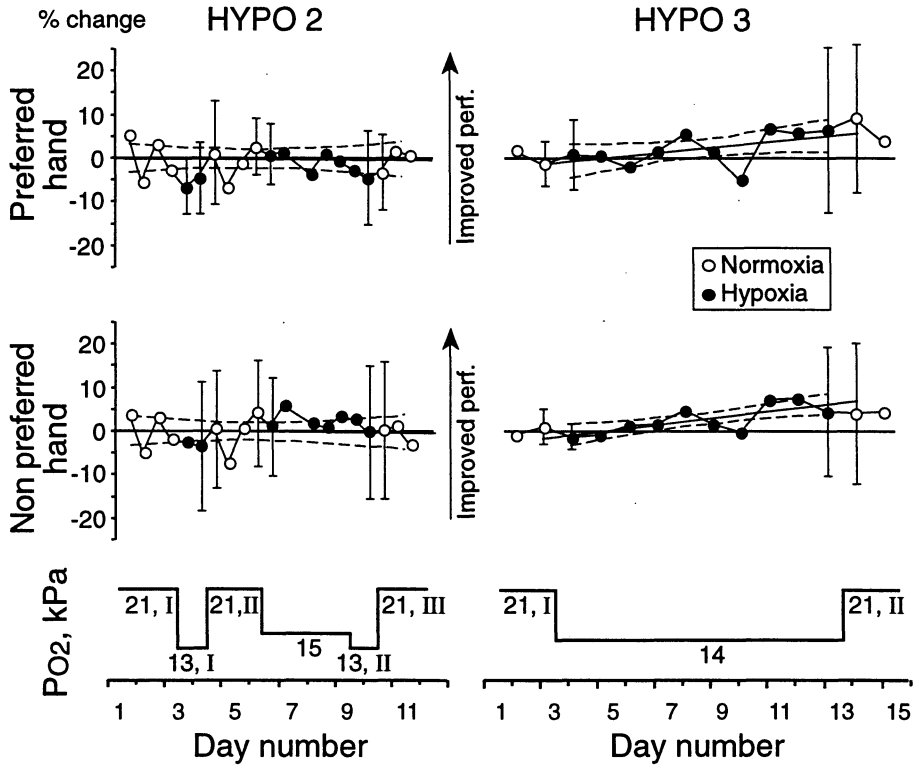


Figure 21 Results from measurements of hand grip strength in HYPO 2 and HYPO 3 are plotted against day of experiment. The change standardized test results are expressed as percentage change from baseline (21 kPa O_2, I); ±1SD are plotted for some test occasions.Regression lines with 90% confidence intervals were calculated from the results in normoxia (HYPO 2). In HYPO 3 the regression lines have been calculated from the results in hypoxia.

4.1.6 Blood analysis

Results from all the blood analyses are presented in Table 11 through 13. Blood sampling occasions are indicated in figure 7. See also Appendix E, "Erythropoietin concentrations during 10 days of controlled normobaric hypoxia" by Bo Berglund, Christina Gustafsson, Hans Örnhagen, and Leif Wide, 1996.

During all three hypoxic exposures there was a significant increase in haemoglobin concentration (B-Hb), erythrocyte concentration (B-EVF) and haematocrit (B-EPK). A small increase in mean corpuscular volume (Ery-MCV), and a small decrease in mean corpuscular haemoglobin concentration (Ery–MCHC) was also seen in HYPO 2 and HYPO 3. In HYPO 1 and HYPO 2 there was also a significant increase in both thrombocyte and leucocyte concentration.

The number of reticulocytes increased in the initial measurements in hypoxia; after 54 hours in 15 kPa O_2 (HYPO 1) and after 24 hours in 13 kPa O_2 (HYPO 2). However, in HYPO 3 blood was not sampled until the fifth day of hypoxia (14 kPa O_2) and at that time there was no difference in reticulocyte concentration compared to control values. After10 days of hypoxia in HYPO 3 the reticulocyte concentration was halved compared to control values.

Erythropoietin concentration showed a large increase during the first three days of hypoxia whereafter the concentration slowly started to decline (only measured in HYPO 1 and HYPO 3). After 10 days of hypoxia (14 kPa O_2 in HYPO 3) it was still twice as high as the control value.

In HYPO 1 there was a small but still significant change in the electrolytes (not analysed in HYPO 2 and HYPO 3). Sodium (Na^+) and chloride concentrations (Cl^-) increased while carbonate concentration (HCO^-_3) tended to decrease. Calcium, albumin and potassium did not change significantly.

Ferritin concentration decreased significantly during 10 days exposure to 14 kPa O_2, but there were no significant changes in fS-Fe and Orosomucoid concentrations (only measured in HYPO 3).

Table 11. Results from blood analysis in HYPO 1.

P_{O2}-level HYPO 1	21, I Control value	15, I after 54 h.	15 , II after 90 h.	Normal value[n]	
B-EVF	45 ± 3.0	49 * ± 3.7	50 * ± 3.1	42-50	%
B-EPK	5.2 ± 0.4	5.5 * ± 0.5	5.5 * ± 0.4	4.5-5.5	x 10(12)/l
B-Hb	155 ± 12.6	165 * ± 13.5	169 * ± 13.3	140-170	g/l
B-Reticulocytes	103 ± 37	121 * ± 28	126 * ± 30	50-130	x 10(9)/l
B-Leukocytes	6.0 ± 1.0	6.5 ± 1.5	7.6 * ± 1.0	4-9	x 10(9)/l
B-Trombocytes	230 ± 59	260 * ± 75	274 * ± 71	150-400	x 10(9)/l
Ery-MCV	88.3 ± 3.3	88.5 ± 3.0	91.8 * ± 3.4	76-96	fl
Ery-MCHC	341 ± 10	339 ± 9	337 ± 9	320-360	g/l
S-Epo	13 ± 7.8	20 * ± 10.5	17 * ± 10.0	<30	mU/ml
S-Kalium	4.33 ± 0.42	4.31 ± 0.45	4.19 ± 0.43	3.4-5.2	mmol/l
S-Natrium	139.1 ± 1.5	139.8 ± 1.8	140.9 * ± 0.6	135-147	mmol/l
S-Klorid	100.5 ± 1.6	102.4 * ± 1.6	102.1 * ± 1.3	95-110	mmol/l
S-Karbonat	28.8 ± 1.2	26.6 * ± 1.4	27.0 * ± 1.6	24-32	mmol/l
S-Albumin	43.0 ± 5.8	43.5 ± 8.0	44.9 ± 8.1	36-47	g/l
S-Calcium	2.43 ± 0.06	2.48 ± 0.05	2.47 ± 0.07	2.20-2.60	mmol/l

[n] Normal value according to the Dept. of Clinical Chemistry, South Hospital (Södersjukhuset), Stockholm.

* Asterisks indicates significantly changed concentration compared to control value (21 kPa O_2).

Table 12. Results from blood analysis in HYPO 2.

P_{O2}-level HYPO 2	21, I Control value	13, I after 24 h.	21, II after 48 h.	15 after 72 h.	21, III after 48 h	Normal value[n]	
B-EVF	46 ± 3.0	50 * ± 1.7	45 ± 2.1	48 * ± 2.5	47 ± 2.0	42-50	%
B-EPK	5.1 ± 0.4	5.5 * ± 0.2	5.0 ± 0.3	5.3 * ± 0.3	5.3 ± 0.3	4.5-5.5	x 10(12)/l
B-Hb	154 ± 10	162 * ± 6	153 ± 7	162 * ± 8	156 ± 8	140-170	g/l
B-Reticulocytes	99 ± 21	103 ± 12	97 ± 17	132 ± 31	131 ± 17	50-130	x 10(9)/l
B-Leucocytes	6.1 ± 0.6	6.8 ± 1.0	6.4 ± 0.9	6.8 ± 0.8	7.5 * ± 1.0	4-9	x 10(9)/l
B-Trombocytes	221 ± 28	224 ± 27	213 ± 28	224 ± 34	242 * ± 37	150-400	x 10(9)/l
Ery-MCV	89.3 ± 2.8	91.5 * ± 2.7	90.0 ± 3.2	90.4 * ± 3.1	89.5 ± 3.2	76-96	fl
Ery-MCHC	331 ± 16	324 * ± 3	336 ± 4	336 ± 5	333 ± 5	320-360	g/l

[n] Normal value according to the Dept. of Clinical Chemistry, South Hospital (Södersjukhuset), Stockholm.

* Asterisks indicates significantly changed concentration compared to control value (21 kPa O_2).

Table 13. Results from blood analysis in HYPO 3.

P_{O2}-level HYPO 3	21 kPa O_2 Control value	Days in 14 kPaO_2 1 day	2 days	3 days	5 days	8 days	10 days	Normal value[n]	
B-EVF	44 ± 2.4	–	–	–	46 * ± 1.7	–	49 * ± 2.6	42-50	%
B-EPK	5.1 ± 0.3	–	–	–	5.3 * ± 0.2	–	5.5 * ± 0.3	4.5-5.5	x10(12)/l
B-Hb	154 ± 8.7	–	–	–	159 ± 5.5	–	168 * ± 9.2	140-170	g/l
B-Reticulocytes	36 ± 20	–	–	–	43 ± 17	–	18 * ± 10	10-100	x10(9)/l
B-Leucocytes	5.9 ± 1.5	–	–	–	6.2 ± 1.8	–	5.7 ± 1.7	4-9	x10(9)/l
B-Trombocytes	250 ± 43	–	–	–	253 ± 41	–	252 ± 44	150-400	x10(9)/l
Ery-MCV	87 ± 2.4	–	–	–	87 ± 2.6	–	89 * ± 2.6	76-96	fl
Ery-MCHC	352 ± 1.4	–	–	–	347 ± 4.9	–	344 * ± 4.5	320-360	g/l
S-Epo	10 ± 3.5	30 * ±10.8	34 * ±11.6	25 * ±11.7	15 ± 3.9	17 ± 4.9	19 ± 5.8	<30	U/l
fS-Fe	16.3 ± 5.1	–	–	–	–	–	17.1 ± 8.1	11-32	µmol/l
P-Orosomucoid	0.80 ±0.24	–	–	–	–	–	0.68 ±0.06	0.45-1.15	g/l
S-ferritin	81 ± 47	–	–	–	–	–	45 * ± 32	11-201	µg/l

n Normal value according to the Karolinska Hospital, Stockholm, Sweden.

* indicates significantly changed concentration compared to control value (21 kPa O_2).

4.1.7 RAT

Mean and Standard deviation for each separate oxygen partial pressure period are presented in Figure 22 and Appendix B. There is no clear difference in readaptation time between normoxia and hypoxia. The variations in the data makes it difficult to draw any conclusions. The test was only used in HYPO 1.

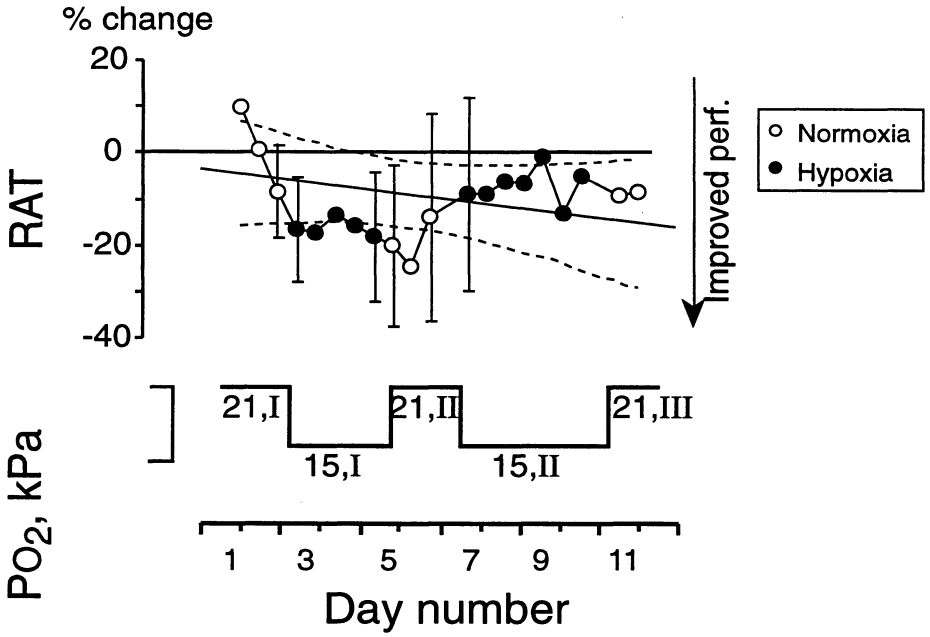


Figure 22. *Results from the RAT measurements in HYPO 1 are plotted against day of experiment. The change in standardized readaptation time (sec) is expressed as percentage change from baseline (21 kPa O_2, I); ±1SD are plotted for some test occasions. Regression line with 90% confidence interval has been calculated from the results in normoxia*

4.1.8 CFF

Mean (M) and standard deviation (SD) for each color and each separate oxygen partial pressure period are presented in Figure 23 and Appendix B. The frequency at which the subject perceived that the stimuli was flickering (CFF) was higher for the green stimuli than for the red ($p<0.01$). Difference in flicker threshold between normoxia and hypoxia was not evident. There was a significant increase in CFF with time in confinement in HYPO 2. However this increase was only seen for the red stimuli. There was no correlation between CFF and performance on cognitive and psychomotor tests or between CFF and the factor alertness on the Environmental Symptoms Questionnaire (ESQ).

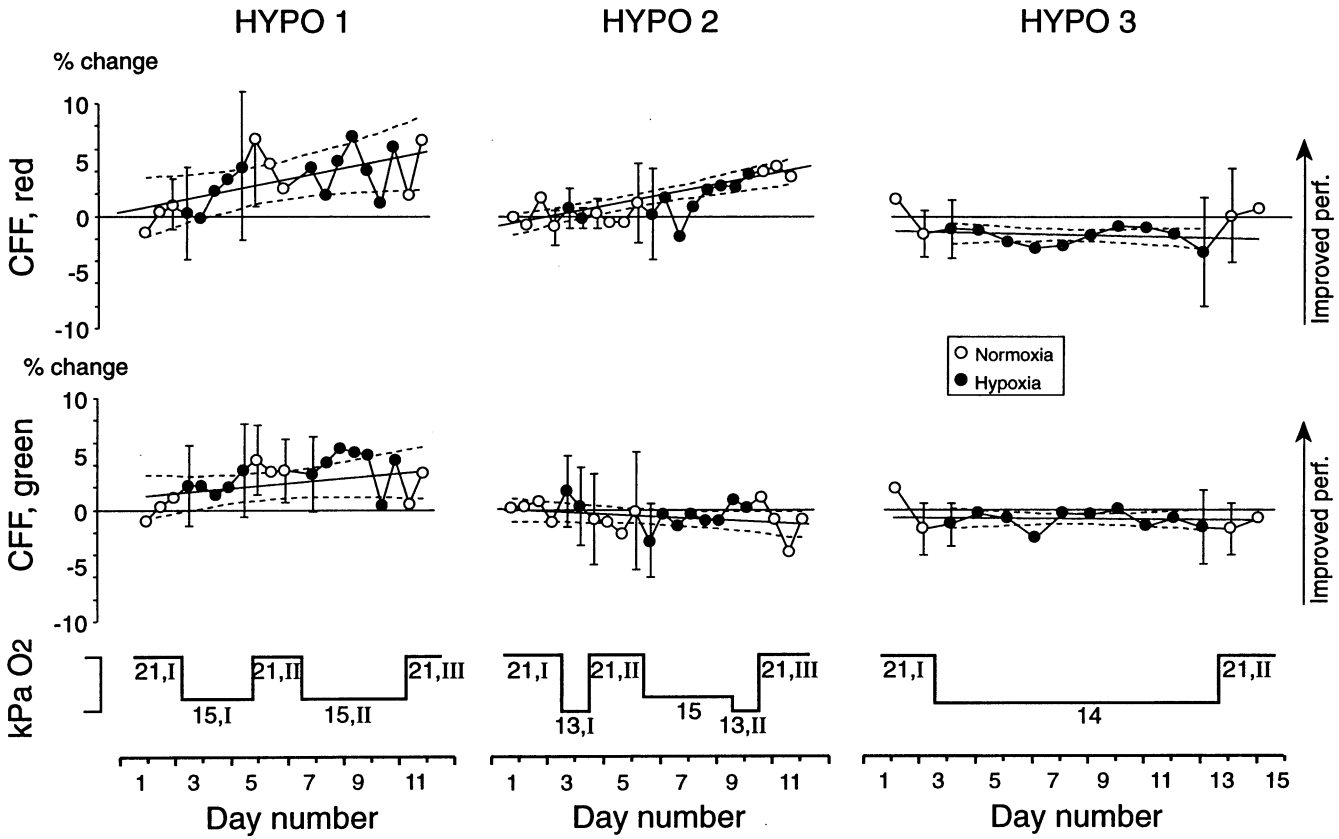


Figure 23. *Results from the CFF measurements in HYPO 1, 2 and 3 are plotted against day of experiment. The change in standardized maximal critical frequency (Hz) is expressed as percentage change from baseline (21 kPa O_2, I); ±1SD are plotted for some test occasions. Regression lines with 90% confidence intervals have been calculated from the results in normoxia (HYPO 1 and 2). In HYPO 3 the regression lines have been calculated from the results in hypoxia.*

4.2 COGNITIVE, PSYCHOMOTOR, AND MOTOR TEST RESULTS

4.2.1 Pre training

In HYPO 1 the subjects practiced the cognitive, psychomotor, and motor tests for six times over a period of two days. In HYPO 2 this number was extended to eight times and in HYPO 3 they had five to six trials on cognitive and psychomotor tests and three trials on the motor tests. In Figure 24 results from both training and experiment period in HYPO 2 is plotted for Grammatical Reasoning, Manikin, and the Finger Tapping test.

In the grammatical reasoning task and in the spatial orientation task (Manikin), learning seems to continue throughout the whole experiment, the major part of learning however, seems to be overcome in eight to twelve trials. For the motor test Tapping changes in the performance with number of performed trials was less obvious, but a slight improvement with time was still evident.

In conclusion, for cognitive tests the number of pre-tests required is very high and confounding of learning has always to be considered in analysis of the data from such tests. The learning curves for some of the motor tests were less steep, but also in these tests the confounding of learning must be taken into account.

4.2.2 Measurements

Group means for the computerized tests are presented graphically in Figure 25 and 26 and group means for the paper and pencil tests are shown in Figure 27 through 29. Results from linear regression analysis, paired *t* tests and ANOVA are presented in Table 14 through 16 respectively. In Appendix C group means and standard deviation for all cognitive, psychomotor, and motor tests are tabulated.

Results from Ravens progressive matrices indicated that there was a difference in mental ability between the three groups of subjects participating in the experiments. In HYPO 1: the group mean and sd was 6.9 ± 1.77, in HYPO 2: 5.5 ± 2.08 and in HYPO 3: 6.5 ± 1.53. Comparisons between the three groups of subjects showed that subjects in HYPO 1 tended to have higher test results on other cognitive tests as well as the highest score on Ravens matrices. There was no significant changes in performance in relation to hypoxia.

Improved performance over time was observed in the majority of tests (see Table 14). However in the motor tests Aiming and Pursuit Aiming and in the 4-choice reaction time test the error rate increased significantly with time and in the Simple reaction time test RT increased with time.

Differences in learning between normoxia and hypoxia were not observed, using paired *t* testing on α and β (see chapter 3.7).

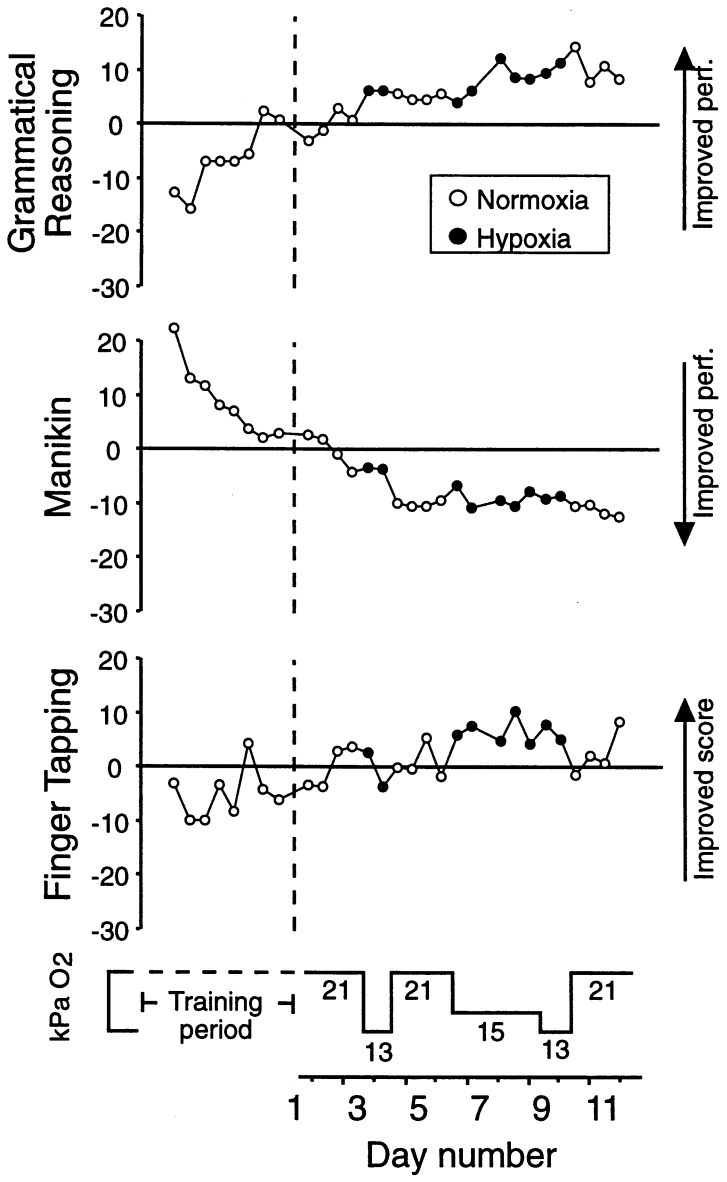


Figure 24. *Results from both training and experiment period in HYPO 2 is plotted against day of testing for Grammatical Reasoning, Manikin, and the Finger tapping test. The changes in results (efficiency, response time, and number of taps) are expressed as percentage change from the baseline (21, 1).*

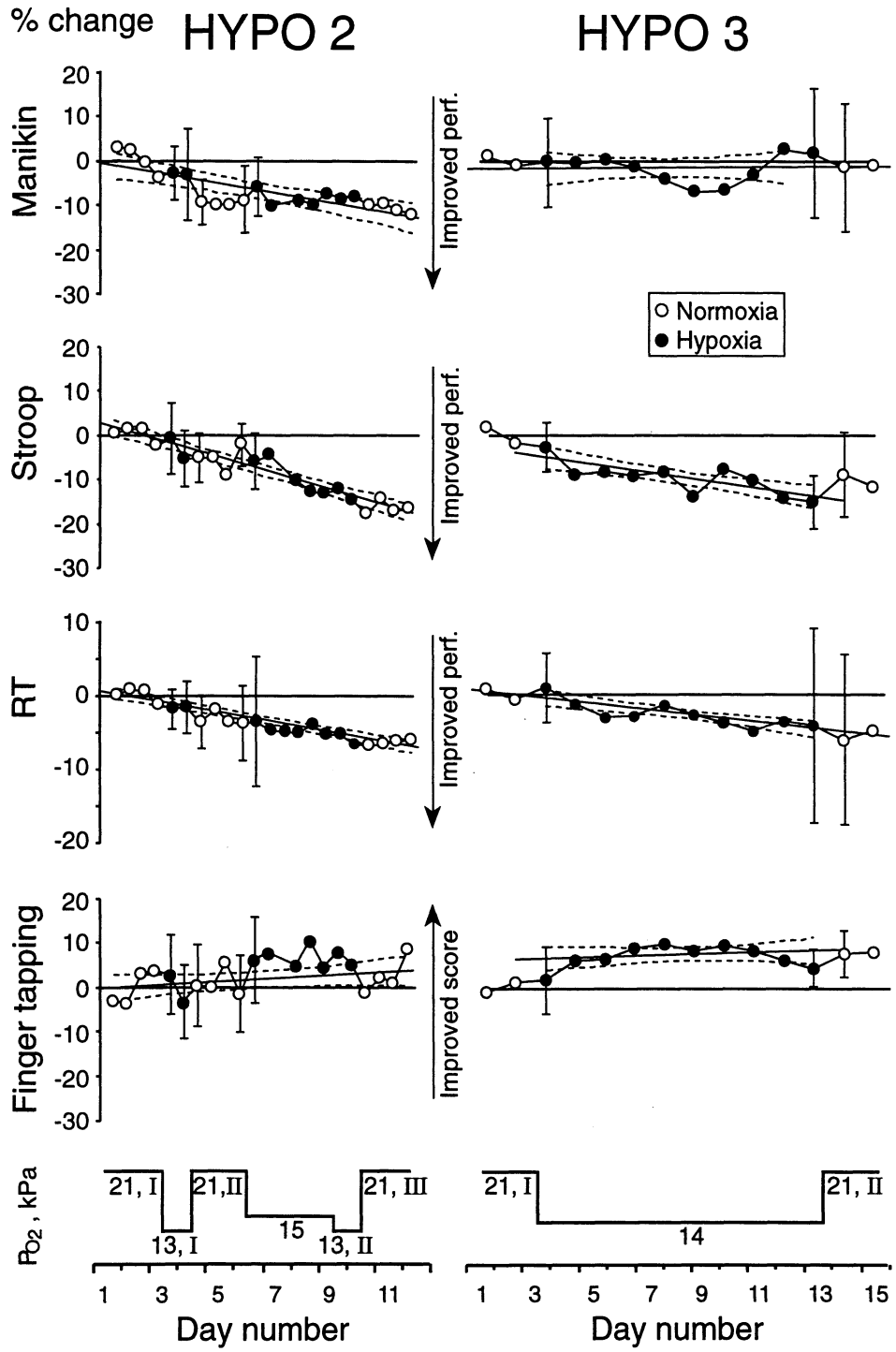


Figure 25. *Results from the computerized tests Manikin, Stroop (naming conflict), RT, and Finger Tapping (preferred hand) in HYPO 2 and HYPO 3 are plotted against day of testing. The changes in results (response time and number of taps) are expressed as percentage change from the baseline (21, I); ± 1SD are plotted for some test occasions. Regression lines with 90 % confidence intervals were calculated from the results in normoxia (HYPO 2) and hypoxia (HYPO 3).*

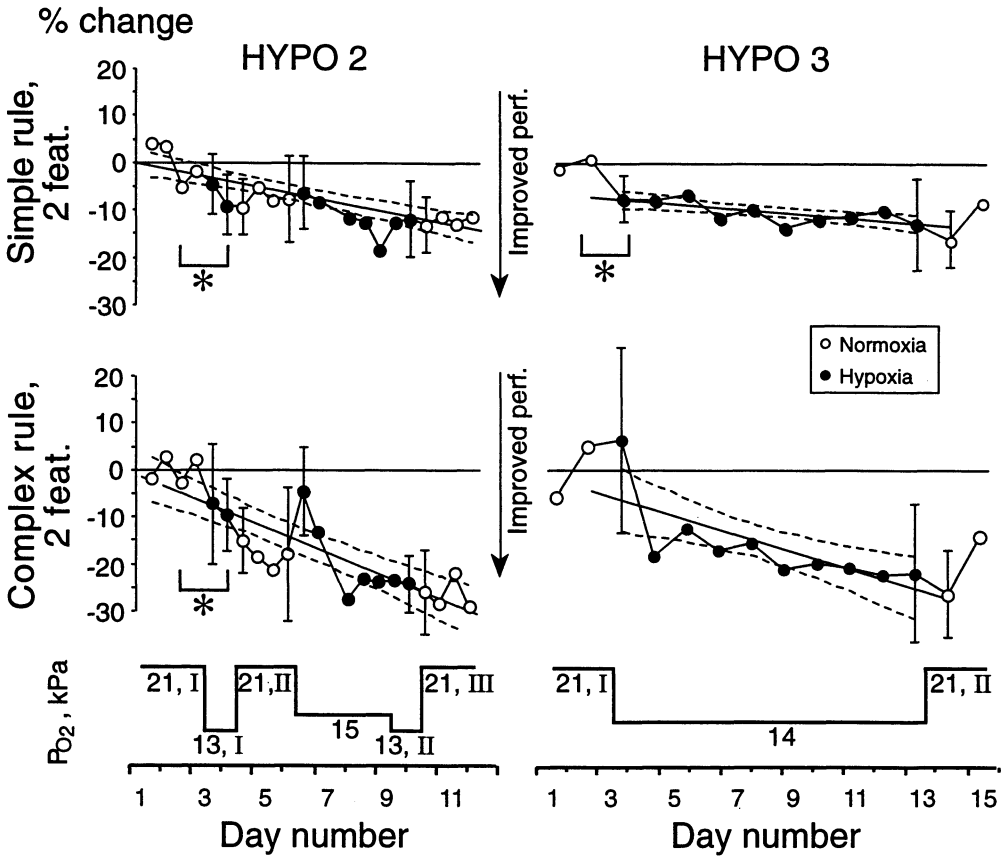


Figure 26. *Results from the Symbol coding task in HYPO 2 and HYPO 3 are plotted against day of testing. The changes in results (response time) are expressed as percentage change from baseline (21, 1); ± 1SD are plotted for some test occasions. Regression lines with 90 % confidence intervals were calculated from the results in normoxia (HYPO 2) and hypoxia (HYPO 3). Asterisks (*) indicates P_{O_2} shifts were paired t tests indicated significantly*

Impaired performance was not seen in any parameter in any of the shifts from high to low oxygen partial pressure and no improvement in performance was seen when P_{O_2} was partial pressure and no improvement in performance was seen when P_{O_2} was increased. In some tests performance even improved during the first shift from normoxia to hypoxia. However, this may have been an effect of learning rather than an effect of hypoxia per se.

Furthermore, none of the performance variables showed significant difference in the overall performance at different oxygen levels (ANOVA), and, thus, did not indicate any impaired performance in hypoxia. For one test variable (Medium Tapping, number correct) improved performance was indicated during hypoxia.

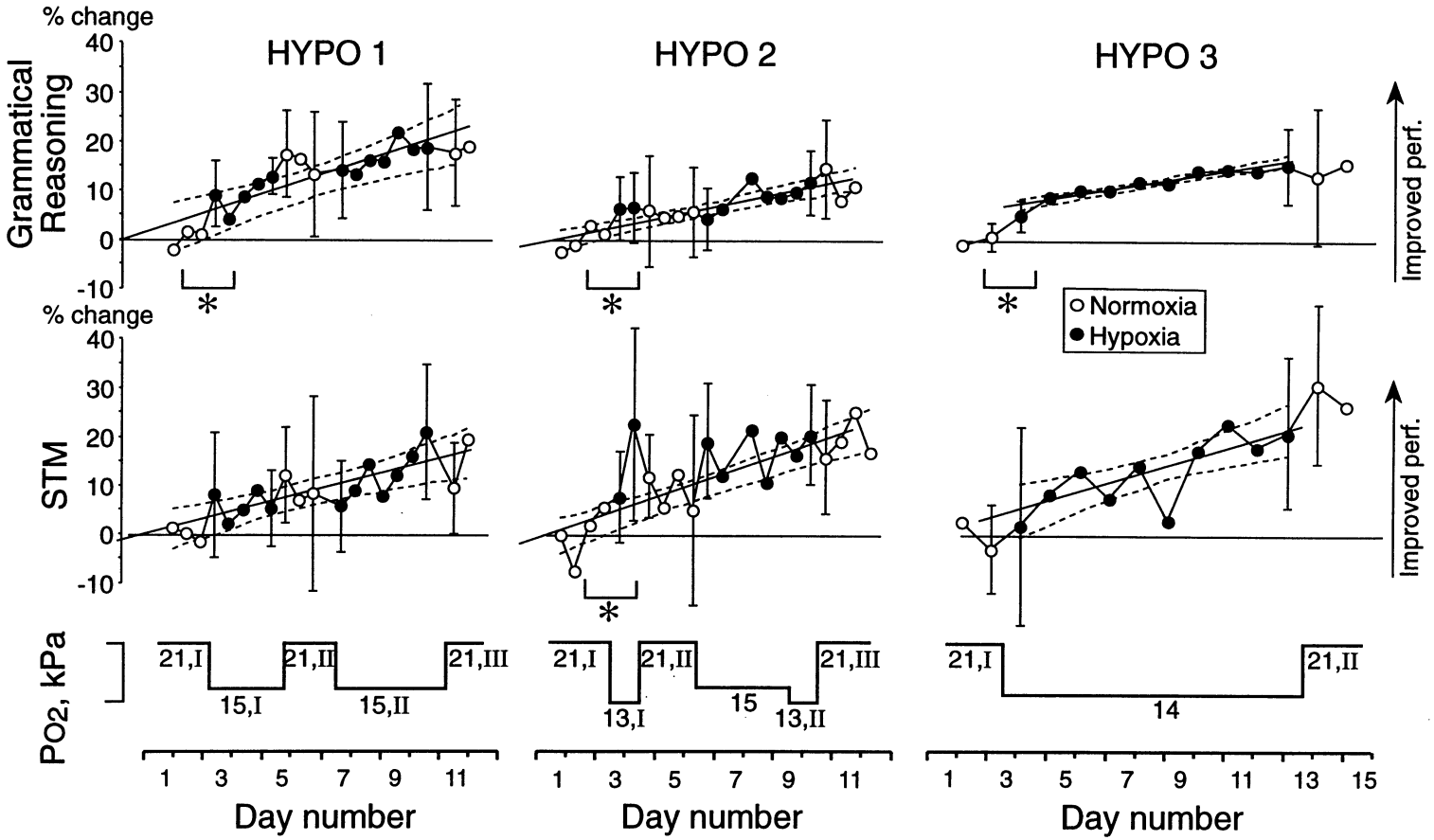


Figure 27. *Results from the tests Grammatical Reasoning, STM, and PASAT are plotted against day of testing. The changes in results (efficiency and number of correct responses) are expressed as percentage change from baseline (21, I); ± 1SD are plotted for some test occasions. Regression lines with 90 % confidence intervals were calculated from the results in normoxia (HYPO 2) and hypoxia (HYPO 3). Asterisks (*) indicates P_{O2} shifts where paired t tests indicated significantly improved performance*

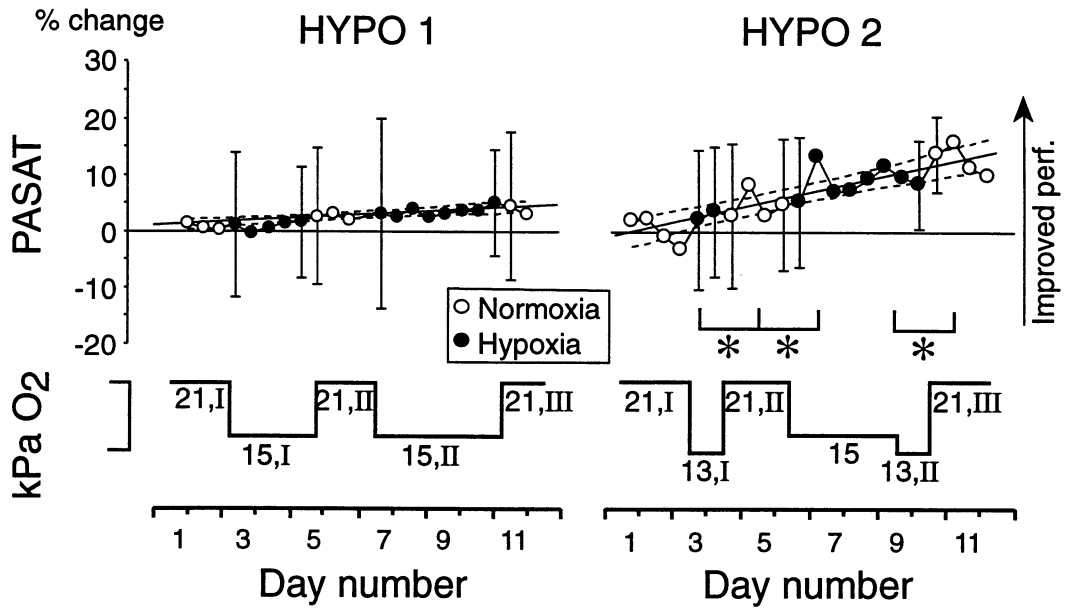


Figure 28. *Results from PASAT (number of correct responses) are plotted against day of testing. The changes in results are expressed as percentage change from baseline (21, I); ± 1SD are plotted for some test occasions. Regression line with 90 % confidence intervals were calculated from the results in normoxia. Asterisks (*) indicates P_{O2} shifts where paired t tests indicated*

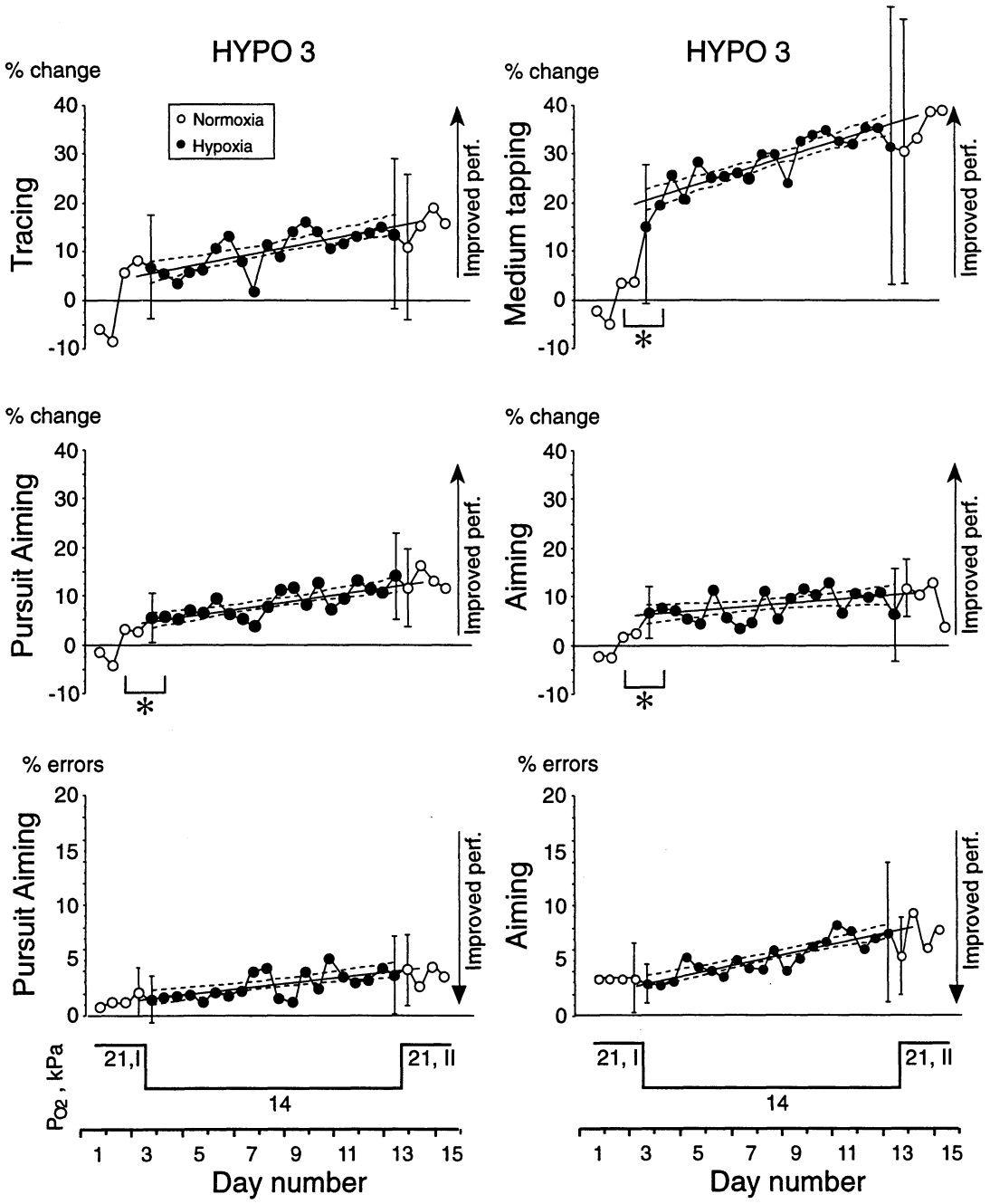


Figure 29. *Results from the paper and pencil tests Tracing, Medium Tapping, Pursuit Aiming, and Aiming are plotted against day of testing. The changes in results (number of correct responses) are expressed as percentage change from the baseline (21, I); ±1SD are plotted for some test occasions. Regression lines with 90 % confidence intervals were calculated from the results in hypoxia. Asterisks (*) indicates P_{O2} shifts where paired t tests indicated significantly improved performance. For Pursuit Aiming and Aiming the error rate is presented as a percentage of the number of attempts.*

Table 14. Results from the linear regression analysis on the overall duration of the experiment.

	HYPO 1	HYPO 2	HYPO 3
Computerized tests			
Manikin, response time	–	** †	ns
error rate	–	ns	** †
Stroop, response time			
congruent, name color	–	** †	ns
congruent, read word	–	** †	* †
conflict, name color	–	** †	ns
conflict, read word	–	** †	ns
control, name color	–	** †	* †
control, read word	–	** †	ns †
RT, response time	–	** †	* †
error rate	–	* #	ns
Finger tapping, number of taps			
preferred hand	–	* †	* †
non preferred hand	–	ns	ns
Symbol coding			
Simple rule, reaction time			
- 1 feature	–	** †	** †
- 2 features	–	** †	** †
Simple rule, accuracy			
- 1 feature	–	** †	ns
- 2 features	–	** †	ns
Complex rule, reaction time			
- 1 feature	–	* †	** †
- 2 features	–	** †	** †
Complex rule, accuracy			
- 1 feature	–	ns	ns
- 2 features	–	ns	ns
SPES: Swedish performance evaluation system			
Symbol digit, response time	** †	–	–
Simple reaction time	** #	–	–
Tapping, number of taps			
- preferred hand	** †	–	–
- non preferred hand	** †	–	–
Paper and pencil tests			
Raven´s matrises	ns	ns	ns
Grammatical reasoning, efficiency	** †	** †	** †
Short-term memory, number correct	** †	* †	** †
PASAT, number correct	** †	** †	–
Medium tapping, number correct	–	–	** †
error rate	–	–	ns
Pursuit aiming, number correct	–	–	** †
error rate	–	–	** #
Aiming, number correct	–	–	** †
error rate	–	–	** #
Tracing, number correct	–	–	** †
error rate	–	–	ns

* P<0.1 ** p< 0.01,
† Improved score/performance,
# Impaired score/performance

Table 15. Results from the paired t-testing over the first shift from normoxia to hypoxia.

	HYPO 1	HYPO 2	HYPO 3
Computerized tests			
Manikin, response time	–	ns	ns
Stroop, response time			
congruent, name color	–	ns	* †
congruent, read word	–	ns	* †
conflict, name color	–	ns	ns
conflict, read word	–	ns	* †
control, name color	–	ns	* †
control, read word	–	ns	* †
RT, response time	–	ns	ns
Finger tapping, number of taps			
preferred hand	–	ns	ns
non preferred hand	–	ns	ns
Symbol coding			
Simple rule, reaction time			
- 1 feature	–	* †	ns
- 2 features	–	* †	* †
Simple rule, accuracy			
- 1 feature	–	ns	ns
- 2 features	–	ns	ns
Complex rule, reaction time			
- 1 feature	–	* †	ns
- 2 features	–	ns	ns
Complex rule, accuracy			
- 1 feature	–	ns	ns
- 2 features	–	ns	ns
SPES: Swedish performance evaluation system			
Symbol digit, response time	ns	–	–
Simple reaction time	ns	–	–
Tapping, number of taps			
- preferred hand	* †	–	–
- non preferred hand	ns	–	–
Paper and pencil tests			
Raven´s matrises	ns	ns	ns
Grammatical reasoning, efficiency	* †	* †	* †
Short-term memory, number correct	ns	* †	ns
PASAT , number correct	ns	ns	–
Medium tapping, number correct	–	–	* †
Pursuit aiming, number correct	–	–	* †
Aiming, number correct	–	–	* †
Tracing, number correct	–	–	ns

* Statistically significant change ($p<0.1$)
† Improved score/performance
\# Impaired score/performance

Table 16. Results from the analysis of variance (ANOVA) for repeated measurements.

	HYPO 1	HYPO 2	HYPO 3
Computerized tests			
Manikin, response time	–	ns	ns
Stroop, response time			
congruent, name color	–	ns	ns
congruent, read word	–	ns	ns
conflict, name color	–	ns	ns
conflict, read word	–	ns	-
control, name color	–	ns	-
control, read word	–	ns	-
RT, response time	–	ns	ns
Finger tapping, number of taps			
preferred hand	–	ns	ns
non preferred hand	–	ns	ns
Symbol coding			
Simple rule, reaction time			
- 1 feature	–	ns	ns
- 2 features	–	ns	ns
Simple rule, accuracy			
- 1 feature	–	ns	ns
- 2 features	–	ns	ns
Complex rule, reaction time			
- 1 feature	–	ns	ns
- 2 features	–	ns	ns
Complex rule, accuracy			
- 1 feature	–	ns	ns
- 2 features	–	ns	ns
SPES: Swedish performance evaluation system			
Symbol digit, response time	ns	–	–
Simple reaction time	ns	–	–
Tapping, number of taps			
- preferred hand	ns	–	–
- non preferred hand	ns	–	–
Paper and pencil tests			
Raven´s matrises	ns	ns	ns
Grammatical reasoning, efficiency	ns	ns	ns
Short-term memory, number correct	ns	ns	ns
PASAT , number correct	ns	ns	–
Medium tapping, number correct	–	–	* †
Pursuit aiming, number correct	–	–	ns
Aiming, number correct	–	–	ns
Tracing, number correct	–	–	ns

* Statistically significant change ($p<0.1$)

† Improved score/performance

4.3 SUBJECTIVE QUESTIONNAIRES AND SUBJECTIVE DATA

4.3.1 ESQ

Data from the questionnaires were evaluated separately for respiratory symptoms, central nervous system problems, symptoms from ear nose and throat, fatigue, and alertness. Group mean (M) and standard deviation (SD) for the different factors at each consecutive oxygen partial pressure level are presented in Appendix H. Results from the ESQ (respiratory and cerebral factor) in HYPO 1 , HYPO 2, and HYPO 3 are presented in Figure 30.

In HYPO 1 no consistent significant differences on the group level were found. However, it seems as if one or two subjects in each watch were affected by the reduced oxygen level (15 kPa), at least for the subscales cerebral and respiratory symptoms.

In HYPO 2 the weighted average for the respiratory symptoms (AMS-R) and the cerebral symptoms(AMS-C) rose significantly when switching from normoxia to hypoxia (13 $kPaO_2$ I). At that occasion three subjects exceeded the limit for acute mountain sickness on respiratory symptoms (0.6 for AMS-R and 0.7 for AMS-C).

The weighted average for alertness factor was significantly lower in the first 13 kPa period than in the normoxia periods. None of the three factors changed significantly during the second period of 13 kPa. Alertness was the only factor that showed significant variations within the day. Team B who carried out tests between 06-12 and 18-24 felt more alert in the morning than in the evening.

In HYPO 3 fatigue was the only factor that increased significant with time in the chamber. Fatigue was the factor that exhibited the best correlation with performance variables.

4.3.2 Mood scale

Group mean (M) and SD for the mood states activity and stress at each consecutive oxygen partial pressure level are presented in Appendix H.

In HYPO 1 ratings for the mood state activity decreased significantly with time in the chamber but there was no relation between mood states and change in the oxygen partial pressure in HYPO 1 and HYPO 2. In HYPO 3 ratings for both activity and stress decreased significantly with time in the chamber.

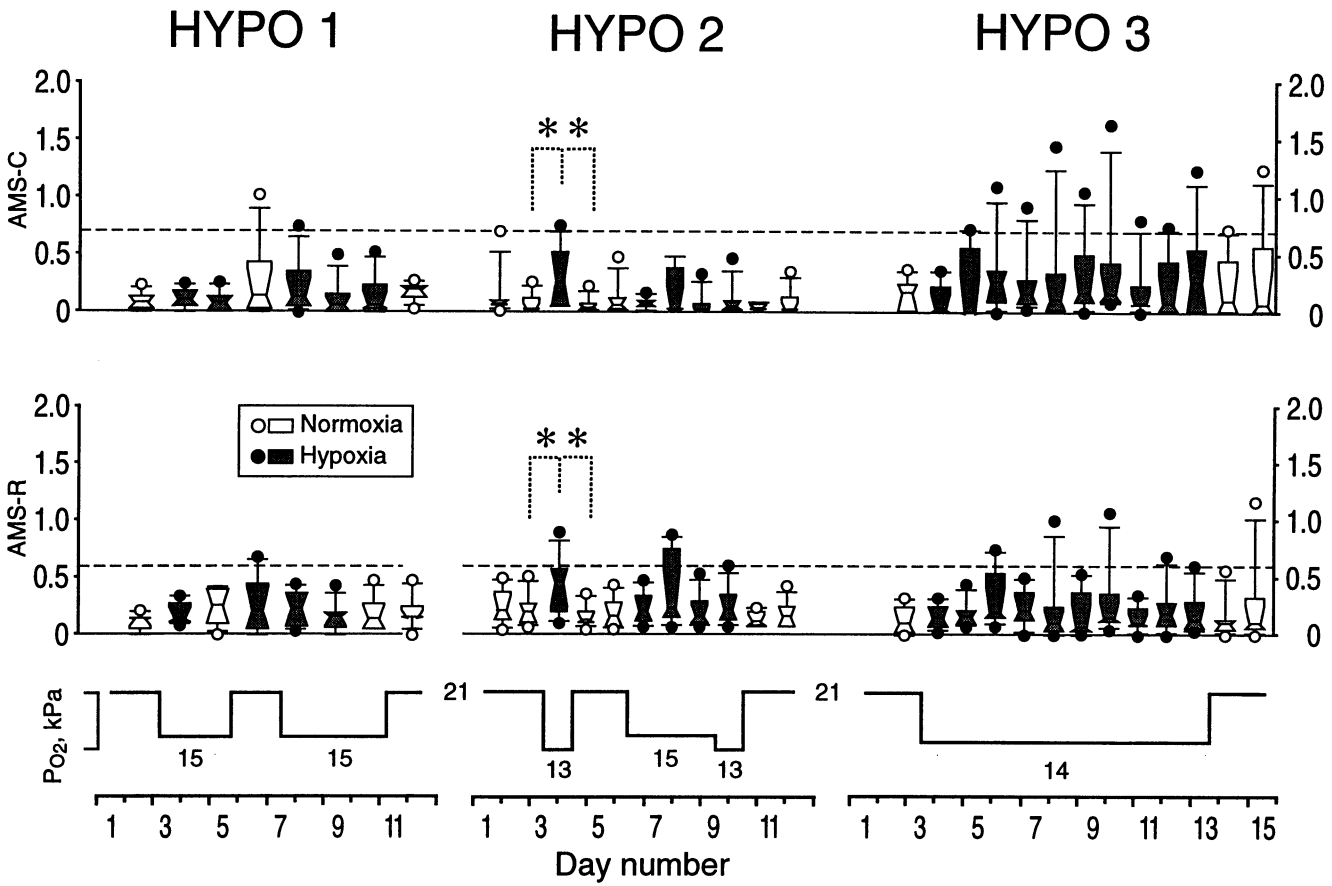


Figure 30. *Results from the ESQ in HYPO 1, HYPO 2, and HYPO 3, plotted as median (notch) for each consecutive 24 hour period. The boxes represents 50% confidence bands and the whiskers (T) represents 90% confidence bands about the median. Individual values above the 90th and below the 10th percentile are indicated by circles. Values above the dashed lines are normally associated with symptoms of AMS (Sampson et al, 1983). Asterisks (*) indicates P_{O_2} shifts were paired t tests or ANOVA indicated significantly changed scores.*

The extended version of the mood scale that was added to the test protocol on the first day of the hypoxic period in HYPO 3 did not show any significant changes in the different dimensions that could be related to hypoxia or daily rhythm (morning vs. evening shift or afternoon vs. night shift), even though there was a significant difference between the two groups. In one of the dimensions, tension, ratings increased significantly with time in confinement.

4.3.3 Sleep and alertness questionnaire

Neither subjective sleep quality nor subjective sleepiness were affected by the oxygen level. Subjective sleepiness increased over the experiment. The reason for this is unclear but might be explained by the long exposure to the confined and monotonous situation. The night watch had more difficulties waking up. However, the group differences should be interpreted with great caution, since the numbers of subjects were very few. For more information see Appendix C, "Sleep duration, subjective sleep quality and sleepiness/alertness" by Mats Gillberg.

4.3.4 Personality dimensions

4.3.4.1 EYSENCK

The mean level of extraversion scores for the subjects in HYPO 1 was 14.3 and the range was 9-20, in HYPO 2 the group mean was 14.3 and ranged from 8-20. In the HYPO 3 group the mean was 16.0 with a range of 14-18. The mean and standard deviation for the extro/introversion scores of a non-clinical Swedish norm group (n=111) have been found to be 13.0 and 3.4 respectively (Bederoff-Petersson, Jägtoft, & Åström, 1968).

4.3.4.2 ADJECTIVES

Group mean (M) and SD for the five personality dimensions before confinement and after 12 days of confinement are presented in Appendix H. None of the personality dimensions changed significantly when comparing the mean before confinement with the mean after 12 days of confinement.

4.3.4.3 CPRS

Statistically significant changes were found in 4 out of 67 items. They were: elation, increased sexual interest, derealisation, and assumed reliability of ratings. For more information see Enclosure D, "Psychiatric ratings of volunteers during stay in a pressure chamber" by Thomas Eklund, Tove Gunnarsson, and Conny Nordin.

5 DISCUSSION

The experiments described in this report were undertaken to investigate the effects of normobaric hypoxia on mental capacity. Results from the cognitive, psychomotor and motor tests have also been presented in separate articles (Linde et al 1997; Gustafsson et al 1997).

Oxygen deficiency is known to impair the mental efficiency but, as was shown in Tables 3 and 4 the tolerable lower limit of inspired oxygen partial pressure with regard to mental performance is still uncertain. If atmospheres low in oxygen content are to be used to reduce fire hazard in confined spaces where people are working it is important to know to what extent the oxygen partial pressure can be lowered without affecting the performance of the exposed personnel. These studies were specifically aimed towards investigating the possibility of using hypoxic gas mixtures in submarines. Therefore the experiments were carried out in a simulated submarine environment. Despite the fact that the CO_2-concentration was kept below the hygienic threshold value, 0.5 kPa, and the temperature and the humidity were reasonably comfortable throughout the confinements, the environment imposed other factors such as long term confinement in an enclosed space with relatively little physical activity, lack of day-light, and change in diurnal rhythm which could have had an effect on the performance of the subjects. The periods with normoxia during the confinements allowed us at least partly to control for these confounding factors.

Although the primary concern of these experiments was the effect of hypoxia on the mental performance it is well known that hypoxia has a wide range of systemic physiological effects, affecting ventilation, fluid balance and acid-base status. The physiological responses to hypoxia, both the acute effects and the physiological short-term acclimatisation display large intraindividual differences (e.g. Reeves et al, 1993; Savourey et al, 1994). Difference in systemic response to hypoxia may well affect the individuals ability to cope with mental stress as well as physical work during hypoxia. Regard et al (1991) showed a strong relationship between the severity of acute mountain sickness (AMS) and performance on cognitive tests in a group of climbers shortly after reaching altitude, and it is not unlikely that also less severe manifestations of systemic physiological effects of hypoxia will affect the mental performance. The acute physiological effects of hypoxia as well as evidence of acclimatization were studied in the subjects, both during rest and during exercise, to be able to assess the impact of the hypoxia and investigate if there was a correlation between physiological effects and decrement in mental performance.

Exposure to hypoxia elicits a compensatory increase in erythrocyte concentration in the blood which facilitates the transport of oxygen from the lungs to the tissues. The rapid rise in red blood cell count is due to a combination of release of erythrocytes and reticulocytes into the bloodstream and fluid shifts from the intravascular space into the interstitial and/or the intracellular space (Rock et al, 1993). The initial increases in

haematocrit, haemoglobin concentration, and red blood cell count seen in HYPO 1-HYPO 3 were of the same magnitude as those reported in earlier studies (Böning, 1970; Luft, 1965).

Apart from redistribution of fluid and blood cells hypoxia also induces an increase in erythropoiesis. The release of factors enhancing the erythropoiesis are initiated already after very short periods of hypoxia. Knaupp (1992) showed that the plasma concentration of erythropoietin (epo) increased when breathing an hypoxic gas mixture (10.5 kPa O_2) for only 2 hours intermittently during a 4-h period. A rapid increase in epo was seen also during HYPO 3 when epo concentration was found to be significantly increased after 24 hours in 14 kPa O_2. The initial increase in epo concentration seen in HYPO 1 and HYPO 3 was of similar magnitude to levels observed during mountain sojourns at comparable oxygen pressures (Gunga et al, 1996). The decrease in epo from its maximum levels that was observed after 5-10 days is also in agreement with previous measurements during hypobaric hypoxia (Gunga et al, 1994; Gunga et al, 1996). The reduction in plasma concentration of ferritin which was seen after 10 day exposure to 14 kPa O_2 (HYPO 3) indicating a decrease in iron stores is a further sign of increased erythropoiesis.

Erythropoietin is thought to exclusively increase the production of erythrocytes. The increase in leucocyte concentration that was seen during the confinements is probably due to haemoconcentration and reaction to upper respiratory tract infections.

The decreased oxygen concentration also causes an increase in ventilation and heart rate. Some of the subjects noted the increased effort to move about in the chamber system during the hypoxia periods. However, all the subjects were able to carry out the physical work that was required of them during the hypoxia. The increase in ventilation and the resulting decrease in end-tidal P_{CO_2} were of the same magnitude as has been observed by other authors studying subjects at similar inspiratory P_{O_2} (e.g. Huang et al, 1984; Reeves et al, 1993; Sato, Severingshaus, & Bickler, 1994). The ventilation continued to increase during the hypoxia periods, and this was reflected by a further decrease in end-tidal P_{CO_2}. This is part of the acute acclimatization to hypoxia (Reeves et al, 1993; Sato, Severingshaus, & Bickler, 1994).

Reeves and coworkers (Reeves et al, 1993) were the first to show that at sea-level the minute ventilation during rest, as reflected by the end-tidal P_{CO_2}, correlated both with the resting ventilation at altitude and the arterial oxygen saturation (S_{aO_2}) at altitude. Subjects with a low end-tidal P_{CO_2} at sea-level, and thus a high ventilation, responded briskly to the hypoxic challenge at altitude with a relatively high increase in ventilation. A high ventilatory response to an hypoxic challenge serves to maintain the oxygenation, which explains the correlation between the end-tidal P_{CO_2} and the S_{aO_2}. However, during rest the correlations between end-tidal P_{CO_2} at sea-level versus end-tidal P_{CO_2} and S_{aO_2} at altitude were rather weak, only corresponding to about 25% of the intra-individual variation (Reeves et al, 1993). In the present studies, during exercise the correlations between end-tidal P_{CO_2} during normoxia and end-tidal P_{CO_2}

and S_{aO_2} during hypoxia were stronger and could account for between 50 - 85% of the individual variation. There was also a weak correlation between end-tidal P_{O_2} in normoxia and end-tidal P_{O_2} during the first hypoxic exposure. However, despite the difference in oxygenation between the subjects during the hypoxia periods no significant correlations between ESQ-scores and end-tidal P_{CO_2} or S_{aO_2} were found. Savourey, Moirant, and Bittel (1994) found a significant negative relationship between end-tidal P_{O_2} during normoxic breathing, both during rest and during submaximal exercise, and ESQ-scores at altitude. However, their altitude observations were carried out at more than 6,000 m above sea-level, which resulted in a much large range of ESQ-scores than in the present study (Savourey, Moirant, & Bittel 1994).

The fact that in a number of investigations a correlation between ventilation at sea-level and at altitude has been found supports the hypothesis that there exists a significant hypoxic drive also during normoxia (Reeves et al, 1993, Savourey, Moirant, & Bittel, 1994).

Training at altitude is known to increase the physical performance at altitude (Terrados et al, 1988). However, the effect of altitude training on performance at sea level is more uncertain, and seems to depend on factors such as absolute altitude, the length of the altitude sojourn, the amount and intensity of training at altitude (both in absolute terms and relative to the amount of training normally carried out at sea-level), and level of fitness (Levine, Roach, & Houston, 1992). The 10 days in hypoxia during HYPO 3 was probably too short a period to be able to induce any definite effect of hypoxic training. The training intensity may also have been too low, and the confinement in itself will have a negative effect on the physical performance. In fact the average increase in physical working capacity (PWC), although not statistically significant, was actually larger in the control group than in the exercise group. It should be noted, though, that due to an infection the fittest subject in the control group had to be withdrawn from the study, making the two groups badly matched with respect to physical fitness.

No differences in cardiac dimensions or systolic function using ultrasound echo-cardiography were found when comparing pre- and post-hypoxia measurements in HYPO 3. In contrast Svedenhag et al (1994) reported a significant increase in oxygen uptake after their return to sea-level, and also found an increased left-ventricular mass, calculated from echo-cardiographic measurements in elite nordic skiers after a 30-day exercise-study at altitude. The fact that the training intensity was lower and the duration shorter in HYPO 3 probably explains the difference in findings between these studies.

In HYPO 3 there was, however, evidence of a change in diastolic function after the hypoxic confinement, with a significant reduction in early trans-mitral flow velocity. This can in principle be caused by either a venous return or a decreased diastolic relaxation. There was some evidence of dehydration, with increased haematocrit and reduced body weight in our subjects after the confinement, which could have caused

a reduced venous return. However, doppler measurements of flow velocities are critically dependent on the angle of insonation. The fact that the ratio of early-to-late diastolic filling velocities did not differ between pre-and post-measurements reduces the physiological significance of this finding.

Ekg-studies during a simulated ascent to the top of Mt Everest (8,848 m) did not show any evidence of cardiac hypoxia (Malconian et al, 1990). The heart appears to be well protected against hypoxia in young and healthy subjects. It was therefore expected that the ekg-recordings in our experiments should remain normal. However, one subject in HYPO 2 showed a depression of the ST-segment in the modified aVF-lead. Although, an ST-depression in this lead usually is not afforded any clinical significance, the fact that there appeared to be a trend towards an increasing depression (Fig 18) caused some concern. However, the relationship between the ST-depression and the hypoxia was far from clear. A normal ekg was recorded during the first period in 13 kPa oxygen, but, the depression started to occur during a 72 h period in 15 kPa oxygen. After having been allowed to rest outside the chamber for a couple of hours the ekg was normal both during air-breathing and when breathing a nitrogen-oxygen mixture containing 15% O_2. A clinical exercise cardiogram performed in normoxic air was also normal. When readmitted into the chamber and exposed to 13 kPa oxygen for 24 h the ekg remained normal. Apart from a minor respiratory infection and a slight feeling of fatigue the subject reported no subjective symptoms. It appears then that this unspecific ekg observation was not directly related to the hypoxia. However, one is to take care if hypoxic atmospheres are to be used in working environments where older people, statistically more prone to ischemic heart disease, will be employed.

Another factor, apart from the hypoxia, which could have affected the performance of the subjects was the change in diurnal rhythm and the subsequent fatigue. During the trials half of the subjects (team A) had to perform work during the night, and shift their main sleep period to the morning hours (0600 -1200). Based on the measurements of body temperature there seemed to be an adjustment to the new diurnal rhythm during the second half of the confinements. The temperature reductions seen after the new main sleep period were larger in HYPO 3 than in HYPO 1 and HYPO 2. This is probably due to the fact that the subjects had to carry out physical work during the night-shift in HYPO 1 and HYPO 2. Only in HYPO 2 was there any difference in subjective symptoms between team A and B, with team A displaying slightly higher scores on the ESQ with regard to three groups of symptoms (A-B: cerebral + 0.3, respiratory + 0.3, and fatigue + 0.6, $p < 0.06$-0.01). There was, however, no difference in performance between the two groups. On the other hand, subjects in team B (HYPO 2) showed a significant effect from time of day. They were more efficient and their RTs were shorter between 18 00 and 0000 than between 0600 and 1200 (Linde et al, 1997).

Other physiological effects of hypoxia which have a more direct bearing on the performance of the operators are the effects on vision. It is known that night vision is affected at altitudes above 3,000 m, corresponding to approximately 15 kPa oxygen.

Also, other aspects of visual performance are known to be perturbed by hypoxia. Tengroth et al (1976) reported that hypoxia (9 and 15% O_2) caused a concentration dependent increase in glare recovery time after photo stress. During HYPO 1 the glare recovery time was tested by measuring the readaptation time (RAT) after a flash. During the second hypoxia period in 15 kPa O_2 the readaptation time was slightly longer than during the surrounding normoxia periods, but the difference was not statistically significant. In Figure 31 the results of Tengroth et al (1976) are plotted together with the results from HYPO 1. It can be seen that the results obtained in HYPO 1 are well within the range of the earlier results showing a tendency towards a slightly increased RAT during hypoxia, but with the limited degree of hypoxia the expected difference in RAT is less than 1 second.

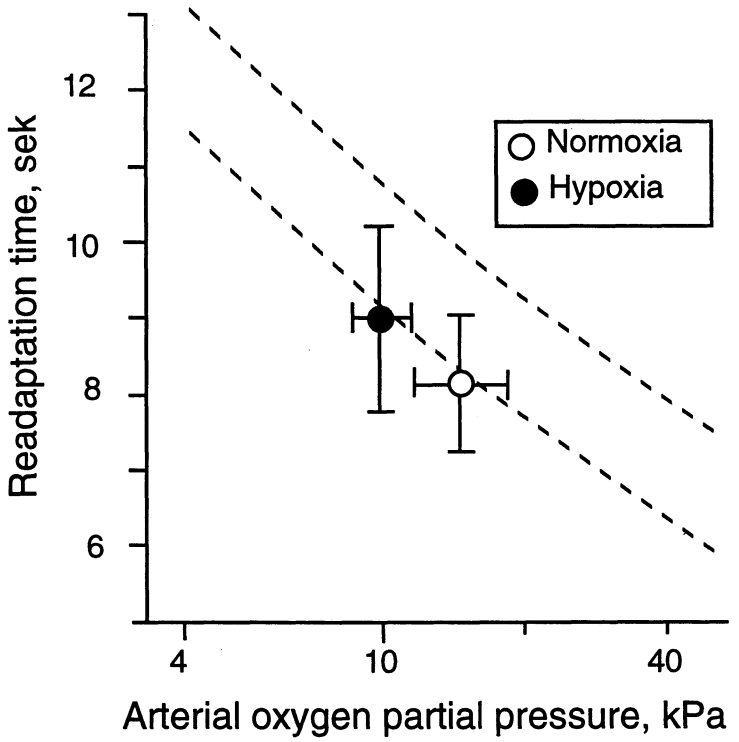


Figure 31. *Optical readaptation time (RAT) after photo stress as a function of arterial oxygen partial pressure. Redrawn from Tengrot et al, 1976. Indicated in the figure are M ± 1 SD for RAT and alveolar oxygen partial pressure obtained in HYPO 1 (P_{IO_2} 21 and 15 kPa).*

The critical flicker fusion frequency did not show any difference between normoxia and hypoxia. It was thought that during a long period of hypoxia (as in HYPO 3) a decrease in sleep quality might result in a decrease in the critical flicker fusion frequency with time. However, although there was an increase in sleepiness with time

in confinement there was no decrease in CFF with time in hypoxia nor was there any correlation between CFF and subjective evaluation of fatigue (ESQ). There was, however, a consistent difference between red and green flicker frequency, with a higher fusion frequency for the green light. Brandl, Frank, and Lachemayr (1993) showed that with decreasing P_{O2} the light intensity must be increased from the sea level intensity, and that there is a tendency towards green colour deficit with the Nagel anomaloscope at low P_{O2}. Since the luminosities of the LEDs used for the CFF were not measured it is not possible to say if the difference in critical frequency between the red and green colour was due to a difference in luminosity or some other factor.

In conclusion the subjects were able to cope with both the degree of hypoxia and the length of exposure to hypoxia with only very limited physiological effects. An increased erythropoiesis and slightly increased rate of ventilation and heart rate were seen. However, the subjects were able to perform physical work at relatively high work intensities. No clear evidence of decrements in visual performance was seen. Also the subjective evaluation of the hypoxic stress only indicated a minor increase in discomfort scores.

The effects of the reduced inspiratory oxygen partial pressure on performance on cognitive, psychomotor, and motor tests were unexpectedly small in these experiments. Even learning, which has been considered to be sensitive to hypoxia (Denison, Ledwith & Poulton 1966; Kelman & Crow 1969; Farmer et al 1992) appeared to be unaffected in HYPO 1-3. Performance in most of the tests improved with time, despite the fact that the subjects stayed for up to 10 days in an environment with only 14 kPa O_2 or for up to 24 hours in 13 kPa O_2. Only in one test, the simple reaction time test used in HYPO 1, did performance decline with time spent in confinement, but since there was no relationship between P_{O2} and reaction time, the observed decline in result was most likely due to the length of the test (6 min) and the fact that the test was repeated so many times that the subjects started to lose their motivation.

It is difficult to interpret what effect the large number of repeated test sessions might have on measurements of cognitive and psychomotor performance. Most likely the mental load of the tests decreased with time, and consequently the sensitivity of the tests might have been reduced with the large number of repeated test sessions. It should also be noted that it is the early part of the learning process that is most sensitive to hypoxia (Denison, Ledwith, & Poulton, 1966; Kelman & Crow, 1969; Farmer et al, 1992). However, performance was maintained or improved also in tests that were administered only a few times, for instance Raven's matrices.

The frequent repetition of the tests could also have a possible decremental effect on the performance in that the repetitions in combination with the long confinement started to bore the subjects. The MOOD protocol was used to assess the motivation of the subjects, which held up surprisingly well during these experiments. To deal with the distraction at the end of the confinements, the chamber stays were ended one day earlier than the subjects had anticipated.

Lack of impairment or even improvement during hypoxia, despite diminished functions, might result from a more careful and concentrated cognitive style among the subjects, due to awareness of their predicament, as discussed by Regard et al (1991). Ledwith et al (1970) came to similar conclusions and suggested that the subjects presented with short tests made an extra effort for the duration of the test and thereby masked impairment which might have been shown by prolonged testing without obvious time limits.

In our study special care was taken not to disclose to the subjects what gas they were breathing. However, some subjects felt physical signs of a changed oxygen concentration (e.g. increased heart rate and shortness of breath during hypoxia). This was most pronounced during the first hypoxic period in HYPO 2 (13 kPa O_2), and even if the subjects were not informed when shifts in P_{O2} took place they might have been aware of the risk of impaired performance and have made an extra effort for the duration of the tests (3 to 12 minutes).

In some motor test the proportion of errors and the speed at which the subjects performed the tests increased with time in confinement. Even though the subjects were instructed to perform as fast and as accurately as possible, they speeded up the rate and became less careful, in contrast to the suggestion of a more careful and concentrated cognitive style in hypoxia (Regard et al, 1991).

Green and Morgan (1985) detected increased error rate on a logical reasoning task performed at 3,600 m (approximately 13.7 kPa O_2). They found it reasonable to suppose that although the subjects were performing worse, they had not realised that they were doing so, since they did not slow their rate of work to match their reduced competence (Green & Morgan, 1985). McCarthy et al (1995) found the response time for judgement concerning the orientation of visual stimuli was slower during acute exposures to 2,133 m (approximately 16.4 kPa O_2) and 3,657 m (approximately 16.4 kPa O_2) compared to the results at sea-level, and that accuracy also was lowered at 3,657 m.

The increased proportion of errors that has been observed in the present study could be an effect of hypoxia on the critical judgement of the subjects. However, as the increased proportion of errors continued also during the following period of normoxia, it seems much more likely that the increased error rate was due to a change in performance strategy due to competitiveness among the subjects. This hypothesis was at least partly confirmed when we learned from informal interviews that some of the subjects dealt with the boredom of the confinement by treating the tests as a competition.

Schlichting et al (1988) have suggested that motor tests might be more sensitive than cognitive tasks to the effects of hypoxia. Finger tapping, though, seemed to be relatively unaffected at the P_{IO_2} level of 10-11 kPa (Adler et al, 1950; Kramer, Coyne, & Strayer, 1993) when performance on other tests was considerably impaired by

hypoxia. In fact in HYPO 2 there were indications that performance on Finger Tapping was slightly better in hypoxia than in normoxia (Figure 25). The tendency towards an increase in Finger Tapping frequency was seen also in HYPO 3. In one fine motor test, Medium Tapping (Figure 29), performance was slightly better in hypoxia compared to normoxia ($p < 0.1$ by ANOVA). One possible interpretation of these findings is that inhibition of fine motor control is reduced by hypoxia. However, this is only an hypothesis which requires much further testing before any firm conclusions can be made.

Exposure to 14 and 15 kPa O_2 did not result in significantly increased scores for symptoms of AMS on the ESQ. In 13 kPa O_2 three subjects exceeded the limit for acute mountain sickness (0.6 and 0.7 for AMS-R and AMS-C, respectively), but since they also reported mild symptoms in normoxia it could not be excluded that these symptoms were caused by upper airway infections rather than hypoxia. There was no indication that these subjects performed worse than the other subjects during sojourn in 13 kPa O_2, in fact two of the subjects with the highest AMS-scores did their best performances during the exposure to 13 kPa O_2. These observations seem to support the conclusions by Ledwith et al (1970) and Regard et al (1991) that subjects aware of a diminished performance can make an extra effort for the duration of a short test and thereby mask the impairment.

When the first exposures to hypoxia for all subjects in the three confinements are considered no correlation between ESQ-scores and performance was found except for a weak negative relationship between respiratory ESQ-scores (ESQ-R) and performance on the Baddeley test ($0.05 < p < 0.1$) and a negative relationship between performance on Finger Tapping and fatigue score (ESQ-F, $p < 0.05$). These results may indicate a slight effect of hypoxia on performance, however, with the very mild symptoms experienced by the subjects in HYPO 1 through HYPO 3 it is difficult to differ between effects of hypoxia, mild infection, and confinement as the source of discomfort (cf Murdoch 1995). In comparison with HYPO 2 the range of ESQ-scores was wider in HYPO 3 (Figure 30) mainly because one subject generally tended to give high scores. However, this subject scored high also during the post-hypoxic normoxic period, and it cannot be excluded that the high scores were due to the confinement and effects of minor respiratory infections rather than hypoxia. The significant increase in fatigue scores during HYPO 3, with 10 days of continuous hypoxia, might also be related to the hypoxia, but without any noticeable decline in ESQ-scores during the following period of normoxia the results cannot be separated from the effects of confinement.

None of the acute changes from normoxia to hypoxia caused any statistically significant decrements in performance, when tested using paired *t* tests on groups of seven to eight subjects. In some performance variables, statistically significant improvements were observed following the first shift from normoxia to hypoxia (see Table 15). In all likelihood those results were due to learning effects that had not been overcome by the pre-exposure training. In view of the results from previous studies

(Table 3) improved or unchanged performance at 13 kPa O_2 is somewhat unexpected even though there are a some reports indicating that performance can be unaffected in some tests even if P_{O2} is below 13 kPa (Table 4). However, it must be emphasised that most studies, with the exception of Shukitt et al (1988) and Knight et al (1990) deal with acute exposures (less than 1 h) to hypobaric hypoxia. Shukitt et al (1988) studying 13 subjects during a 15-day exposure to different oxygen levels (21%, 17%, and 13%) concluded that normobaric 13% O_2 may produce short-term decrements in cognitive functions and mood, lasting a day or so, and moderate AMS symptoms in some individuals.

The fact that the resulting hypoxia will be more profound in hypobaria than in normobaria, when breathing the same partial pressure of oxygen (see chapter 2.2) may explain why symptoms of AMS are more severe in hypobaric hypoxia than in normobaric hypoxia (Roach, Loeppky, & Ichenagle, 1996), and may also explain why performance decrements seem to be more pronounced during altitude and simulated hypobaric hypoxic exposures compared to normobaric hypoxic exposures.

There are many factors besides differences in P_{O2} and atmospheric pressure that might account for these differences, such as e.g. carbon dioxide concentration (Knight et al, 1990; Schlichting et al, 1988; Shukitt et al 1988), physical activity (Denison et al, 1966), climate (Regard et al, 1991), undisturbed test conditions (Macintosh et al, 1988), the anxiety of naive subjects sitting in pressure chamber (Paul & Fraser, 1994), the number of pre-exposure training sessions, time interval between training and hypoxic exposure, carbon monoxide concentration, sleep disturbances, and fatigue.

In conclusion exposure to normobaric hypoxia at levels of 14-15 kPa O_2 for several days did not affect psychomotor- or cognitive performance significantly. Nor did exposure to 13 kPa O_2 for 24 h cause significant decrements in performance. However, in some subjects the subjective discomfort ratings exceeded the limits for acute mountain sickness.

6 CONCLUSIONS

Under the conditions tested, cognitive, psychomotor, and motor performance decrements could not be observed even when the inspiratory oxygen partial pressure was as low as 13 kPa. The proportion of errors in some motor tests increased with time in confinement. As this increase continued in the last normoxia period it is much more likely due to the boredom of confinement and a change of performance strategy due to competitiveness among the subjects.

During the first exposure to 13 kPa O_2 (HYPO 2) there was a significant increase in subjective symptom (AMS-C and AMS-R on the ESQ) and some of the subjects noted increased heart rate and ventilation. However they were able to carry out physical work without any impairment (75 % of $\dot{V}_{O_2}$ max for up to 45 min in 14 kPa O_2).

It is necessary to be careful regarding recommendations about the lowest allowable P_{O_2} in confined spaces, since hypoxia in real world situations is likely to appear in combination with other stressors such as contaminated atmosphere, lack of sleep, extreme time pressure, and threat. There is also a need for caution if hypoxic atmospheres are to be used in working environments where older people, statistically more prone to ischemic heart disease will be employed. However, in our experiments the effects of hypoxia did not seem to be any greater than the effect of change of environment, motivation, fatigue, or similar factors.

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APPENDICES

TABLE OF CONTENTS

	TEAM B				TEAM A
Time	**Subj. 5**	**Subj. 6**	**Subj. 7**	**Subj. 8**	**Subj. 1-4**
06.00	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	
06.05	Symbol coding				Breakfast
06.10					
06.15	4-choice RT				
06.20	Stroop				
06.25					SLEEP / REST
06.30	Manikin				
06.35	Tapping				
06.40	CFF				
06.45	STM				
06.50	ESQ / MOOD	Symbol coding			
06.55					
07.00	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	
07.05	Motorik	4-choice RT			
07.10	Baddeley	Stroop			
07.15					
07.20		Manikin			
07.25		Tapping			
07.30		CFF			
07.35		STM			
07.40		ESQ / MOOD	Bicycle ergometry		
07.45			P01		
07.50		Motor tests	EKG		
07.55		Baddeley			
08.00	Temp + Sleepiness	Temp + Sleepiness		Temp + Sleepiness	
08.05	Auditive attention	Auditive attention			
08.10			Temp + Sleepiness	Bicycle ergometry	
08.15				P01	
08.20				EKG	
08.25					
08.30					
08.35	Raven	Raven			
08.40					
08.45	Hand grip	Hand grip			
08.50	strength	strength	Hand grip	Hand grip	
08.55			strength	strength	

	TEAM B				TEAM A
Time	**Subj. 5**	**Subj. 6**	**Subj. 7**	**Subj. 8**	**Subj. 1-4**
09.00	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	
09.05		Bicycle ergometry	Auditive attention	Auditive attention	
09.10		P01			
09.15		EKG			
09.20					
09.25					
09.30					
09.35			Symbol coding	Raven	
09.40					
09.45			4-choice RT		
09.50			Stroop		
09.55					
10.00	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	
10.05			Manikin		
10.10			Tapping		
10.15			CFF		
10.20			STM		
10.25	Bicycle ergometry		ESQ / MOOD		
10.30	P01				
10.35	EKG		Motor tests		
10.40			Baddeley	ESQ / MOOD	
10.45			Raven		
10.50				Motor tests	
10.55	Temp + Sleepiness	Temp + Sleepiness		Baddeley	
11.00			Temp + Sleepiness	Temp + Sleepiness	
11.05	Work at 75 % of VO2 max			Symbol coding	
11.10	for 45 min				
11.15	every other day			4-choice RT	
11.20				Stroop	
11.25					
11.30				Manikin	Sleep questionnaire
11.35				Tapping	
11.40				CFF	Lunch
11.45				STM	
11.50					
11.55	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	Temp + Sleepiness	

Swedish Performance Evaluation System (SPES)

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METHODS

Six different tasks from the computerized Swedish Performance Evaluation System (Gamberale, Iregren, & Kjellberg 1990)). were included in the battery. Two rating scales, one pertaining to symptoms of hypoxia and the other a mood scale, one reaction time test, a coding task, and two motor tests, one finger tapping speed task were included. The tests were administered by the subjects themselves on Toshiba 3200 portable computers, connected to a printer outside the chamber.

The week prior to the start of the experiment the subjects practised at the tasks on a total of six occasions during two consecutive days. The number of practice runs varied between the different tasks, since the tests vary a lot with respect to complexity and sensitivity to training effects. The number of training occasions is mentioned in the following descriptions of each task.

Description of the questionnaires and performance tests

The subjects completed the following test sequence in the order presented at two occasions each day during the experiment.

The Environmental Symptoms Questionnaire (ESQ III)

The Environmental Symptoms Questionnaire was validated in a series of studies of acute mountain sickness (Sampson et al, 1983). The questionnaire contains 67 questions concerning respiratory symptoms, central nervous system problems, symptoms from ear, nose, and throat, fatigue, and alertness. Ratings are made on six point scales with verbal labels, ranging from 0, labelled "Not at all" to 5, labelled "Extreme". The subjects filled out this questionnaire on 2 occasions prior to the experiment.

Simple reaction time
Simple reaction time is a sustained attention task measuring response speed to an easily discriminated but temporally uncertain visual signal. The task is to press a key on the computer key board as quickly as possible when a large red rectangle is presented on the display. A total of 96 stimuli were administered during 6 min at intervals varying between 2.5 and 5.0 s. The first minute serves as practice, after which performance capacity is assessed for 5 min . The subjects were allowed to practice only once with the reaction time test.

Symbol digit
Symbol digit is a revised version of a traditional test of perceptual speed. In one row on the screen a key to this coding task is given by the pairing of symbols with the randomly arranged digits 1 to 9. The task is to key in as fast as possible the digits corresponding to the symbols presented in random order in a second row. Each item consists of 9 pairs of randomly arranged symbols and digits, and a total of ten items are presented. Performance is evaluated for the last six items of the test. The subjects had six full runs with this test prior to the experiment.

Finger Tapping
Finger Tapping measures the maximum rate of repetitive movement. The task is to tap as rapidly as possible on a key at the key board with the index finger. The forearm is kept in a fixed position at the table. A total of eight 10 s trials, with a forced interval of 15 s, are performed while alternating between the preferred and non-preferred hand. Fort trials are given using each hand, and the first trial with each hand is regarded as practice trial. Before the experiment the subjects practised with the finger tapping on 4 occasions.

Self rating of mood
The scale consists of 12 mood descriptive adjectives coupled to a six category response scale (Kjellberg & Iwanowski, 1989). The response categories have verbal labels ranging from "not at all" to "very much". Ratings are given by typing the number of the appropriate response alternative. A score in each scale is computed in two mood dimensions identified by factor analysis, an Aurosal and a Stress dimension. The scales are bipolar with three adjectives representing each pole. The score in each scale is computed as a mean of the ratings of the six adjectives after a reversal of the response scale for the lower pole items.

Statistical tests

Due to the general planning and structure of the experiment, it was not possible to carry out any global analysis of variance on the outcome data. Therefore, significance testing has been performed using a series of t-tests, comparing performance or rating data for each of the two watches during one treatment period to the data from the following treatment period. The same kind of tests was performed also to evaluate the presence of possible circadian variations.

RESULTS

Questionnaires

Environmental Symptoms Questionnaire

Data from the questionnaire were evaluated separately for respiratory symptoms, central nervous system problems, symptoms from ears, nose and throat, fatigue, and alertness. No consistent significant differences on the group level were found. However, as may be seen from the plots of individual ratings of symptoms, it seems that one or two subjects in each watch is affected by the lowered oxygen, at least for the subscales cerebral symptoms and respiratory symptoms.

Self rating of mood

Data from the questionnaire were evaluated separately for the two subscales stress and activity. No consistent significant differences on the group level were found, and there were no indications that any single individual reacted differently from the group.

Performance tests

Results from the performance tests are presented in Figure 1 and in Table 1.

Simple reaction time

No significant performance changes in the expected direction were seen at the group level, and there were no indications that the reaction time of any individual was affected by reduced oxygen levels. Significant circadian variations were observed, with shorter reaction times in the "afternoon" than in the "morning".

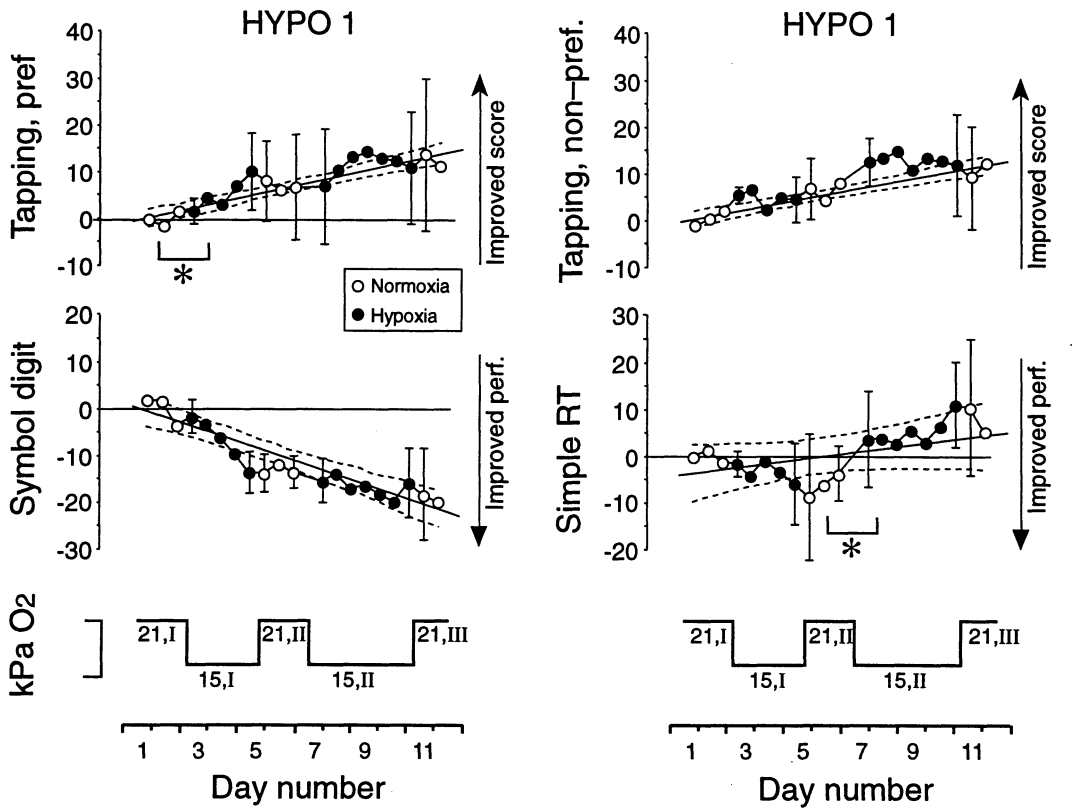

Figure 27. *Results from the computerized SPES test battery are plotted against day of testing. The changes in results (response time and number of taps) are expressed as percentage change from baseline (21, I). Regression lines with 90 % confidence intervals were calculated from the results in normoxia. Asterisks (*) indicates P_{O_2} shifts were paired t tests indicated significantly changed performance.*

Symbol digit

No significant performance changes in the expected direction were seen at the group level, and there were no indications that the latency for the coding performance of any individual was affected by reduced oxygen levels. There is a continuous reduction in mean latencies for the symbol digit coding performance during the entire duration of the experiment.

Finger tapping speed

No significant performance changes in the expected direction were seen at the group level, and there were no indications that the tapping speed of any individual was affected by the lowered atmospheric oxygen content. For one of the two watches there is a continuous increase in the number of taps made over the experimental session.

Table 1. *Mean(M) and standard deviation (SD) for the different tests included in the SPES test battery in HYPO 1. The M and SD for the tests pertain to all test sessions within a specific P_{O_2} level.*

P_{O_2}	M	(SD)	M	(SD)
FINGER TAPPING, no. of taps				
	preferred hand		non-preferred hand	
21, I	71	(8.5)	63	(7.1)
15, I	74	(7.4)	65	(7.2)
21, II	75	(7.0)	66	(6.5)
15, II	78	(7.6)	68	(7.4)
21, III	79	(5.7)	69	(5.2)
SIMPLE REACTION TIME			SYMBOL DIGIT	
	msec		msec	
21, I	221	(17)	1827	(302)
15, I	214	(21)	1669	(260)
21, II	207	(27)	1572	(215)
15, II	233	(24)	1502	(180)
21, III	237	(26)	1461	(199)

DISCUSSION

In general, no effects on performance from the reduced atmospheric oxygen concentration could be observed. Furthermore, it seems that on the group level, no increase in symptoms or changes in mood were found.

However, there are some indications that the symptom reports of a few individuals may be affected by the reduced oxygen contents in the inspired air. Still, these indications suggest quite small changes, and the changes are not fully consistent over the experimental period. There seemed to be an increase in the symptoms reported by a few individuals in relation to the first period of reduced oxygen, but the expected recovery by return to normal oxygen levels was not observed for all subjects reacting, and the reaction indicated at the first period with low oxygen was not repeated for all subjects by the second period at 15% oxygen.

Since for simple reaction time clear circadian variation was observed, it seems that this test showed the sensitivity that has been documented in several applications previously. In earlier studies of effects from various low arousal inducing agents, such as sleep deprivation, solvent exposure, and exposure to noise, it has been shown that this reaction time test is very sensitive. Thus, it does not seem probable that exposure to atmospheric oxygen at 15% causes any decrease in arousal.

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Sleep duration, subjective sleep quality and sleepiness/alertness

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METHODS

Subjective sleep quality was assessed with the Karolinska sleep diary. This instrument has been used in several studies (Kecklund & Åkerstedt, 1993; Åkerstedt et al, 1995) and has been shown to have good correspondence with EEG-recorded sleep (Åkerstedt et al., 1994). The following items from the diary formed the index: "how was your sleep", "unrestful sleep", "difficulties falling asleep", "premature awakening", and "well rested". The index could vary between 1 and 5 (best quality).The Karolinska sleepiness scale (KSS) was used to measure subjective sleepiness. The scale ranges between 1 ("very alert") and 9 ("very sleepy, great effort to keep awake, fighting sleep"). Also this instrument has been validated against objective measurements, for instance, EEG-recordings (Åkerstedt & Gillberg, 1990) and performance (Gillberg et al., 1994).

STATISTICAL METHODS

Data were collapsed over the six successive experimental periods, that is, the first period with 21% O_2, the first period with 13%O_2, the second period with 21% O_2, the period with 15%, the second period with 13% O_2, and the third period with 21%. All data have been analysed with Analysis of variance (ANOVA) for repeated measurements on the factor experimental period (time). In addition, group (A or B) was added as a between factor. Since repeated measurements ANOVAs might violate the assumptions of compound symmetry all p-values are given after Huyn-Feldt's correction.

RESULTS AND DISCUSSION

Sleep duration.

The times for going to bed and for rising, respectively, are mainly a function of the duty schedules for the two groups and are therefore not analysed here. Sleep duration was analysed for the main sleeps, for the nap sleeps and for all sleep obtained during

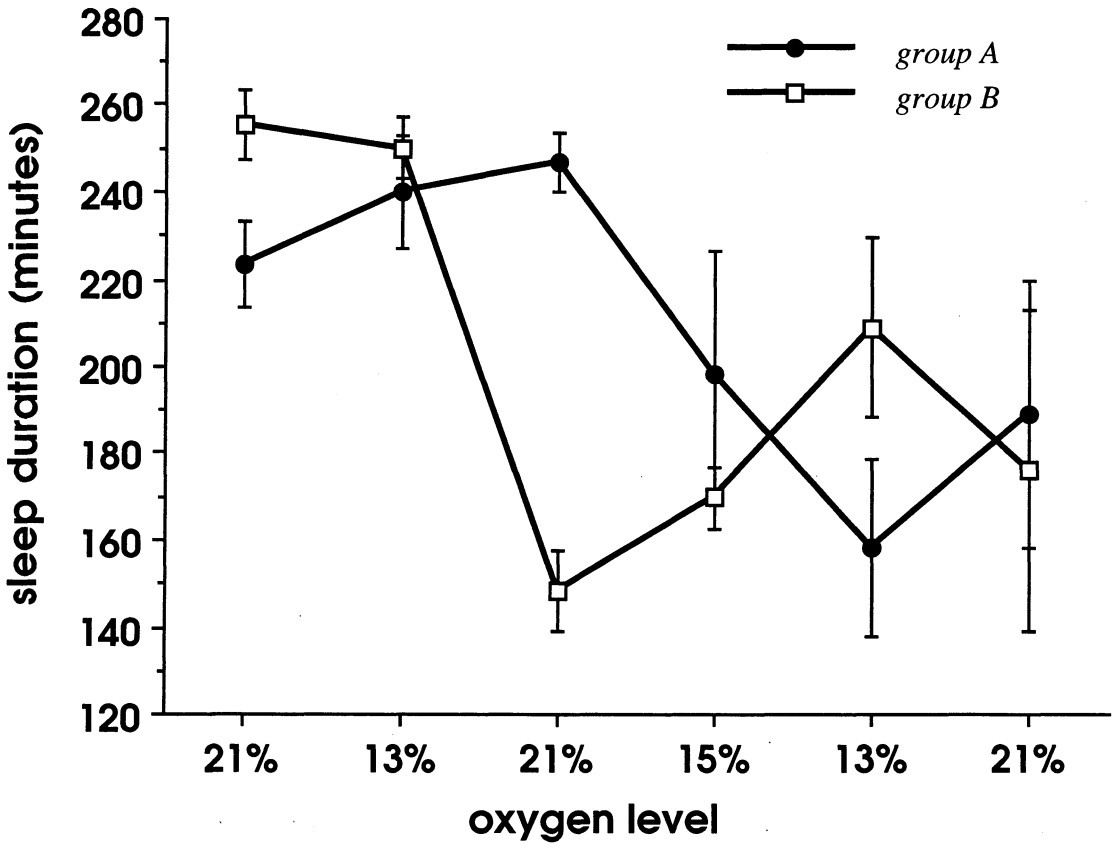

Figure 1. *Main sleep duration (means and standard errors) of group A and group B, respectively, across the experiment. Results from ANOVA: F(group; df 1, 6)= 0.26, ns; F(time; df 5, 30)= 5.45. p<0.01; F(interaction group x time; df 5, 30) = 4.49, p<0.02.*

a 24-hour period, respectively. The subjects in group A had their main sleeps between 06h and 12h, while those in group slept during the interval 00h and 06h. Results from the main sleeps are shown in figure 1, those from the nap sleeps in figure 2, and the total sleep duration per 24 hours in figure 3.

There was no significant group difference for main sleep duration nor for nap sleep duration. Figure 1 shows that the significant change in main sleep duration was a fall across the experiment and the significant interaction explains the different patterns between the groups. An inspection of figure 2 shows that, at least for group B, the subjects compensate shorter main sleep with longer nap sleep. Looking at the amounts

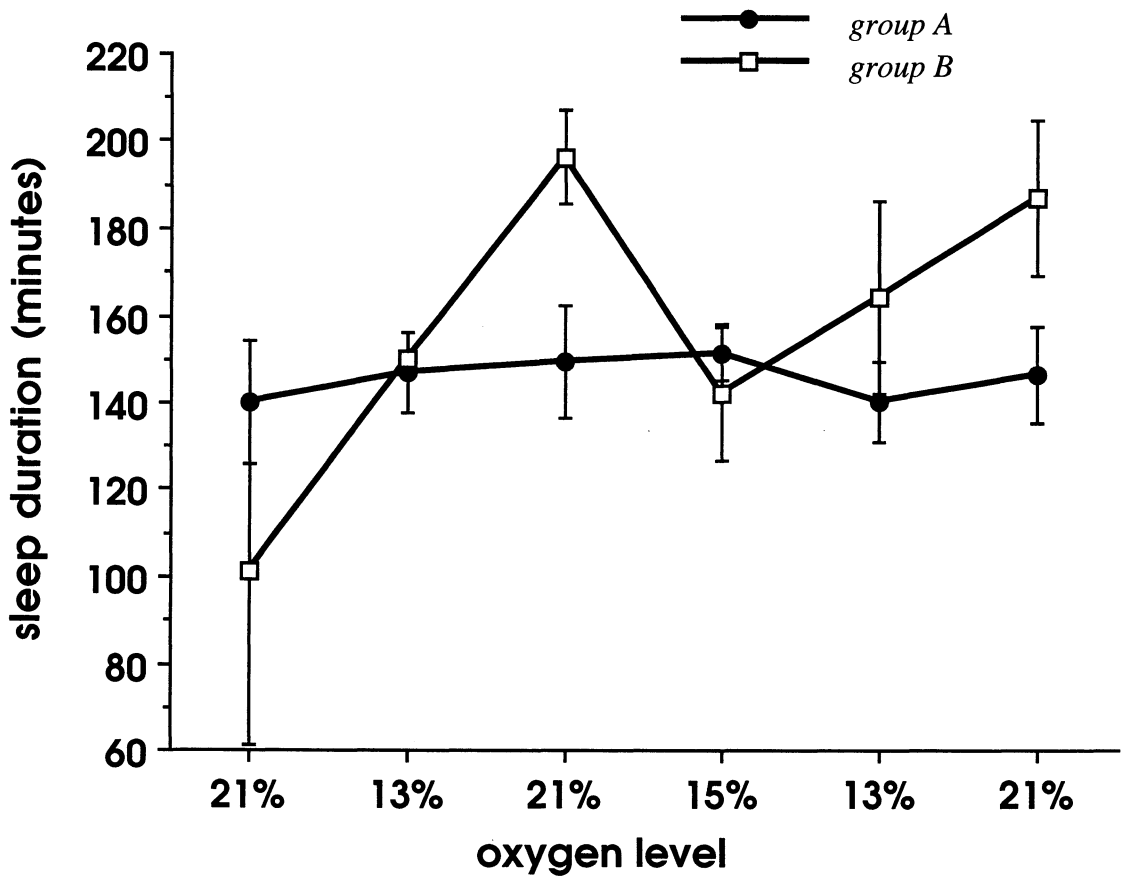

Figure 2. *Nap sleep duration (means and standard errors) of group A and group B, respectively, across the experiment. Results from ANOVA: F(group; df 1, 6)= 0.82, ns; F(time; df 5, 30)= 2.62. ns; F(interaction group x time; df 5, 30)=2.09, p<0.02.*

of sleep obtained in 24 hours, both groups show a similar pattern. Generally, sleep duration increases during the first 4 periods and drops back during the last two periods. It is difficult to ascribe the observed changes in sleep duration to changes in oxygen level, for instance, the final 13% period is similar to the final 21% period. The relative changes noted for the main and nap sleep durations might be a consequence of a gradual adaptation to a biphasic pattern of sleep

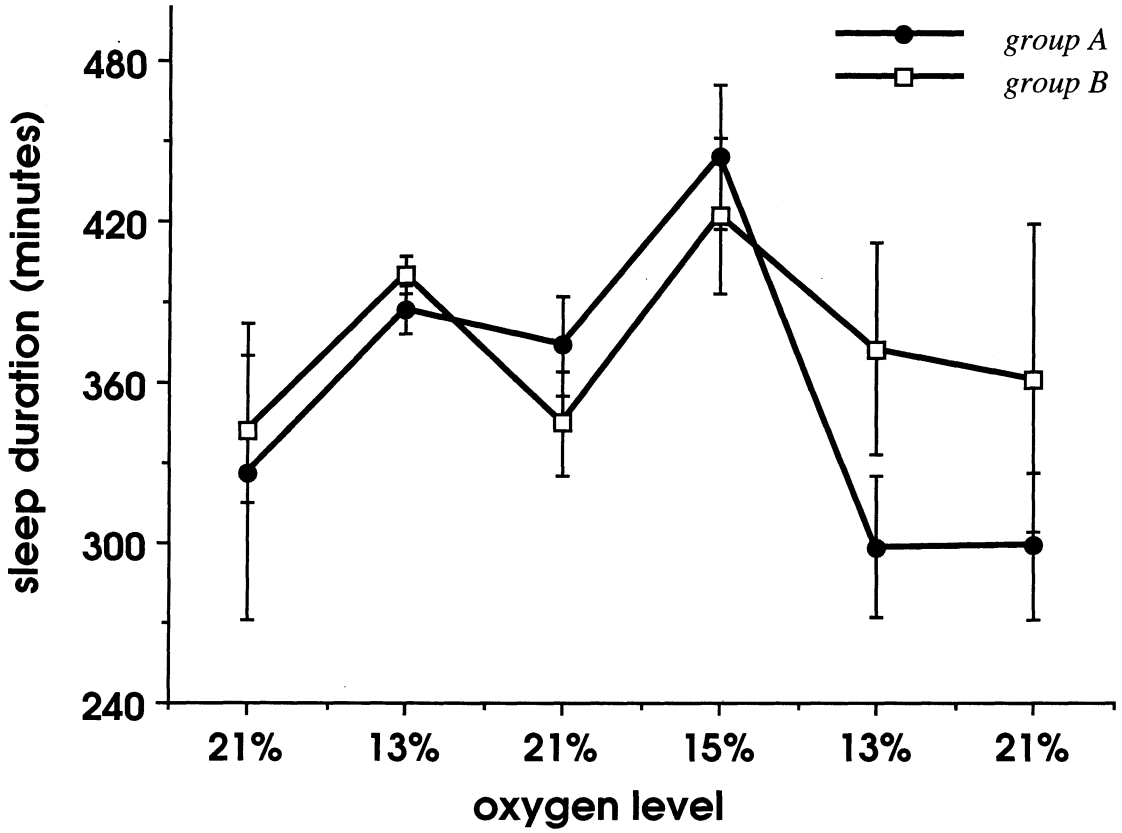

Figure 3. *Total sleep duration during 24 hours (means and standard errors) of group A and group B, respectively, across the experiment. Results from ANOVA: F(group; df 1, 6)= 0.79, ns; F(time; df 5, 30)= 3.88. p<0,02; F(interaction group x time; df 5, 30)=1,03, ns.*

Sleep diary

A sleep quality index was calculated from the sleep diary. Figure 4 shows the data for the main sleeps of the two groups across the experimental periods.

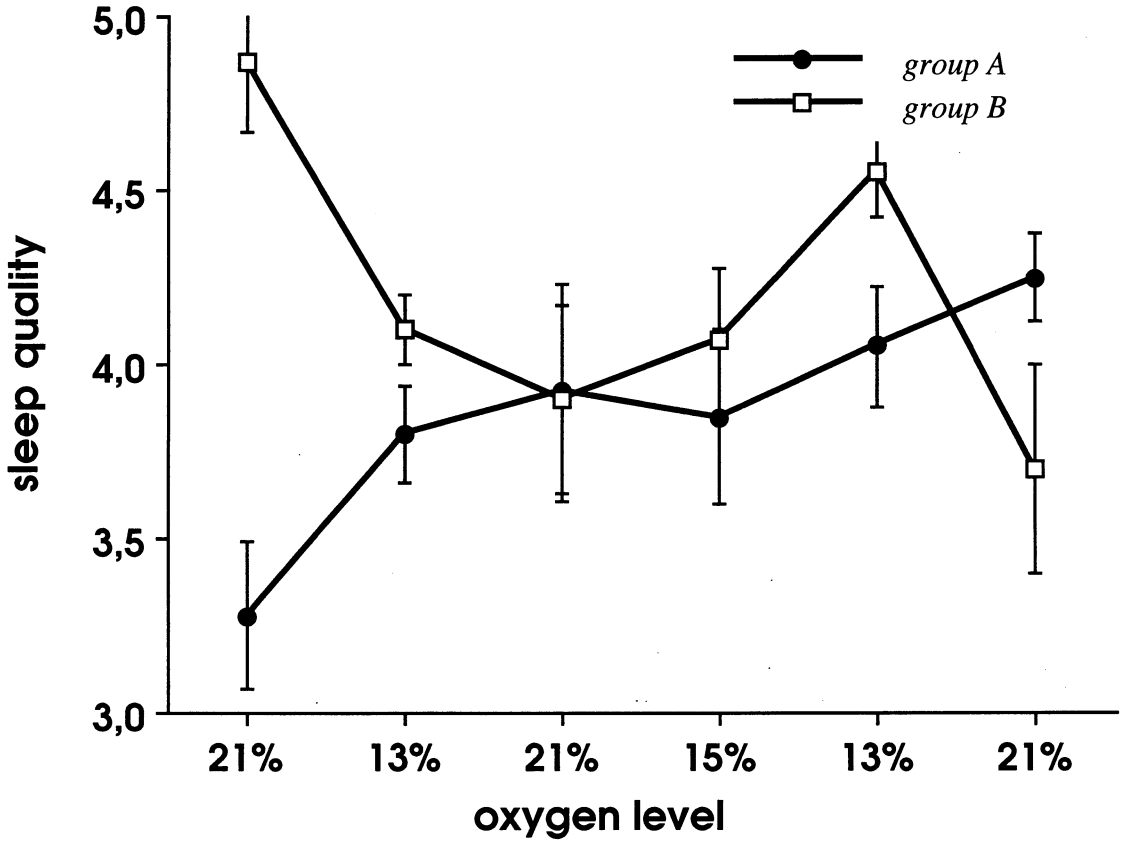

Figure 4. *Sleep quality index (means and standard errors) of group A and group B, respectively, across the experiment. Results from ANOVA: F(group; df 1, 6)= 3.35, ns; F(time; df 5, 30)= 1.20, ns; F(interaction group x time; df 5, 30)=7.30, p<0.001.*

The overall sleep quality was good for both groups, around 4 on the 5-point index, and there was no significant group difference. Neither was there an overall change across the experimental periods (that is, the factor "time"). There was, however, a highly significant interaction and an inspection of figure 4 gives at hand that this might be explained by the large group difference during the first 21%-period. Presumably, this reflects the fact that the subjects in group A during this period were not yet adapted to the imposed sleep/wake schedule with a main sleep during the day. Later on their perceived quality increase. Group B on the other hand maintained the habitual night

sleep pattern and had initially a good sleep quality. There were no evident connections between oxygen level and perceived sleep quality.

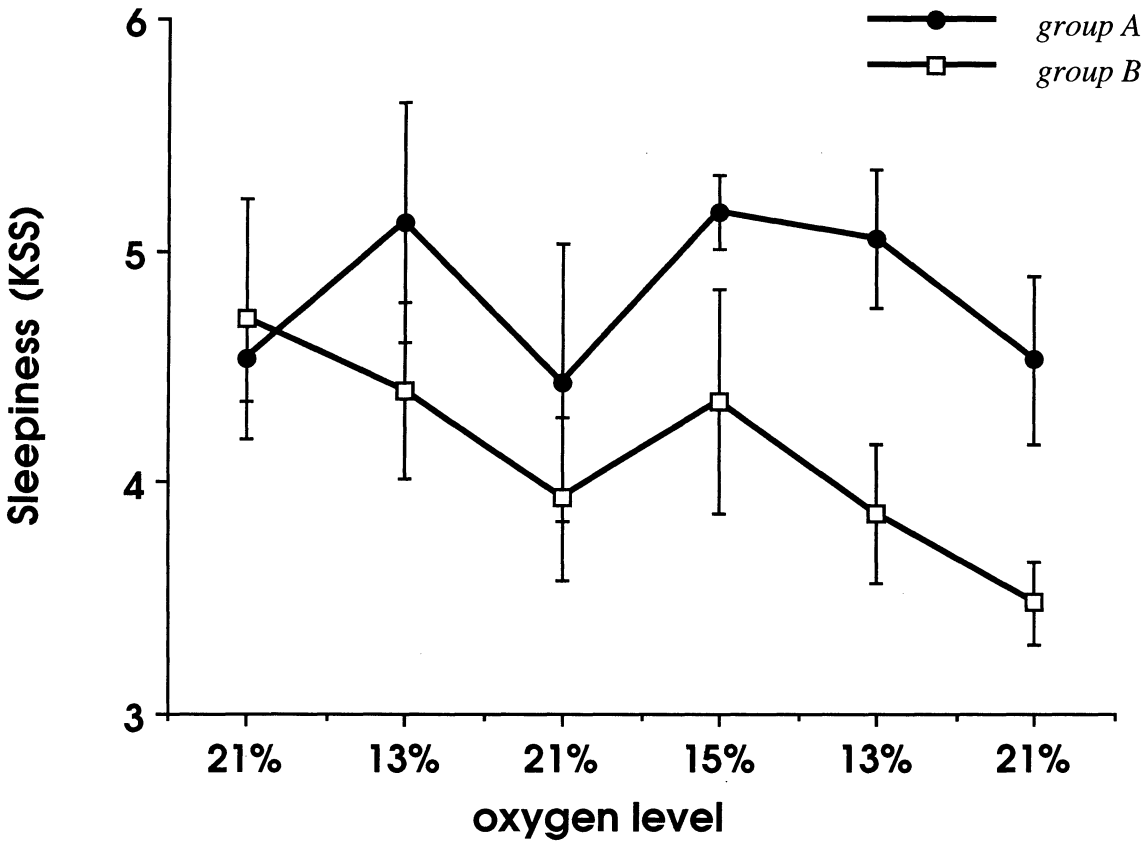

Figure 5. *Sleepiness ratings (KSS; means and standard errors) of group A and group B, respectively, across the experiment. Results from ANOVA: F(group; df 1, 6)= 2.75, ns; F(time; df 5, 30)= 2.51, ns; F(interaction group x time; df 5, 30)=1.37, ns.*

Subjective sleepiness

Subjective ratings of sleepiness across experimental periods are shown in figure 5. For each of the six periods all KSS ratings given every two hours during the 6-hour waking periods were averaged to form single means.

Although figure 5 shows a slight decrease in sleepiness across the experiment and a lower level of sleepiness for group B, no statistical support for this could be found. The overall level of alertness waried between scale values 3 ("alert - normal level") and 5 ("neither alert nor sleepy"), that is, there was no period with significant sleepiness.

CONCLUSIONS

Neither subjective sleep quality nor subjective sleepiness were affected by the oxygen level. The effects that appeared could be attributed to the different timings of sleep/ wake of the two groups and to the adaptation procedure to these schedules. However, the group differences should be interpreted with great caution, since the number of subjects in each group were very few.

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Psychiatric ratings of volunteers during stay in a pressure chamber

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Methods

All the items from the Comprehensive Psychopathological Rating Scale (CPRS)(1) were used in the rating of volunteers before (n=9), during (n=7) and after (n=7) their stay in a pressure chamber. The ratings were performed by dr Tove Gunnarsson and dr Thomas Eklundh, both psychiatrists. Two of dr Eklundh´s volunteers were omitted because of somatic complications. During the stay in the pressure chamber, dr Gunnarssons volunteers were also rated by professor Conny Nordin, Department of Psychiatry, University Hospital, Linköping. As the ratings after half the exposition-time were performed during stay in a pressure chamber, the requirements for "blind technique" were not met.

Non-parametric statistics were used (2). The medians for individual items were not useful for comparisons, as the changes were too small, why range and mean rank are reported.
Friedmans ANOVA was used to detect changes between the three rating sessions. The Wilcoxon signed rank test was used to localize differences between the ratings in case of significance in Friedmans test. Mann-Whitney U-test was used to compare the scores of the two raters .

The level of significance was in all calculations set at $p<0.05$.

Results

The sum of the rating scores increased numerically from session to session, but not significantly (Table 1).
When the separate items were examined, significant differences were found for item 2 (elation), item 22 (increased sexual interest), item 27 (derealisation) and item 67 (assumed reliability of the rating) (Table 2). No further information was obtained when Wilcoxon signed rank test was employed. Results on a trend level ($0.05<p<0.1$) were noted for item 18 (reduced appetite), item 19 (reduced sleep), item 23 (autonomic disturbances), item 30 (disrupted thoughts) and item 32 (ideas of grandeur).

Differences were found between raters (Eklundh - Gunnarsson) for item 27 (derealisation; before), item 23 (autonomic disturbances; during), item 2 (elation; after), item 19 (reduced sleep; after) and for the score sum before the stay in the pressure chamber (Mann-Whitney; $p<0.05$) (Table 3). When the sum of scores during and after the stay in the pressure chamber was expressed as percent of the score before, no difference between the raters was found (during: $z=-1.09$; $p=0.2752$; after: $z=-0.22$; $p=0.8273$).

The simultaneous ratings performed by dr Gunnarsson and professor Nordin during the stay in the pressure chamber confirmed dr Gunnarsson´s ratings. No difference was found for any of the items (Wilcoxon signed rank test).

Discussion

The material comprising seven volunteers who completed the project is for natural reasons small and our results must be interpreted with caution. The risk for type II-errors (lack of conclusive findings due to a small number of subjects) must be taken into consideration.

We found certain differences between items when comparing the three sessions (Table2). The change in item 2 (elation) seems mainly to be due to an increase after the completion of the project, and is probably more of a psychological reaction than an effect of the changed physiological conditions. This reasoning is probably also applicable to item 22 (increased sexual interest) (Table 3).

For item 27 (derealisation) we noted a decrease compared to the rating before the stay in the pressure chamber. This might suggest an effect of the stay itself, but could also reflect negative expectations before the exposure. The fact that the raters differed significantly from each

other regarding this item (Table 3) is difficult to explain. It might be due to the distribution of the volunteers or - which is less probable - a lack of inter-rater reliability. The same discussion is applicable to item 3 and item 19 (Table 3).

The assumed reliability of the rating (item 67) seems to be lower during the stay, which may suggest that the raters were affected by the changed physiological conditions in the chamber. All raters reported increasing fatiguability during the course of the rating.

Conclusion

The changes that were demonstrated for certain items can not with any degree of certainty be related to the changed physiological conditions in the chamber. The number of volunteers is so small that it undeniably affects the possibility to detect differences. Comparison with other parameters in the project such as ESQ might possibly give indications of effects.

In a possible repeated experiment, the inter-rater reliability must be controlled before (and during) the experiment. Furthermore, the rating should perhaps be done from a position outside the pressure chamber, e.g. through a window and using a suitable communication equipment.

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Table 1. Median scores for the sum of 66 items in CPRS

Before	During	After
3	3.5	5

Friedman ANOVA chi corrected for ties=2.30;p=0.3172

Table 2. Range [ ] and mean ranks ( ) for items with significance when tested with Friedmans ANOVA

Item	Before	During	After
2 (elation)	[0-1]	[0-0.5]	[0-2.5]
	(2)	(1.6)	(2.4)
	Chi corrected for ties=6; p=0.0498		
22 (increased sexual interest)	[0-0]	[0-0]	[0-1.5]
	(1.8)	(1.8)	(2.4)
	Chi corrected for ties=6; p=0.0498		
27 (derea-lisation)	[0-1]	[0-0]	[0-0]
	(2.4)	(1.8)	(1.8)
	Chi corrected for ties=6; p=0.0498		
67 (assumed reliability of ratings)	[2-3]	[2-3]	[2-3]
	(2.2)	(1.6)	(2.2)
	Chi corrected for ties=6; p=0.0498		

Table 3. Items for which significant differences were found between raters

	Mean rank			
	TE	TG	Z	p
27(derealisation, before)	6.6	3	-2.91	0.0285
23 (autonomic disturbances; during)	2	5.5	-2.22	0.0262
2 (elation; after)	6	2.5	-2.22	0.0262
19 (reduced sleep; after)	6	2.5	-2.22	0.0262
Sum; before	6.9	2.6	-2.34	0.0195

ERYTHROPOIETIN CONCENTRATIONS DURING 10 DAYS OF CONTROLLED NORMOBARIC HYPOXIA.

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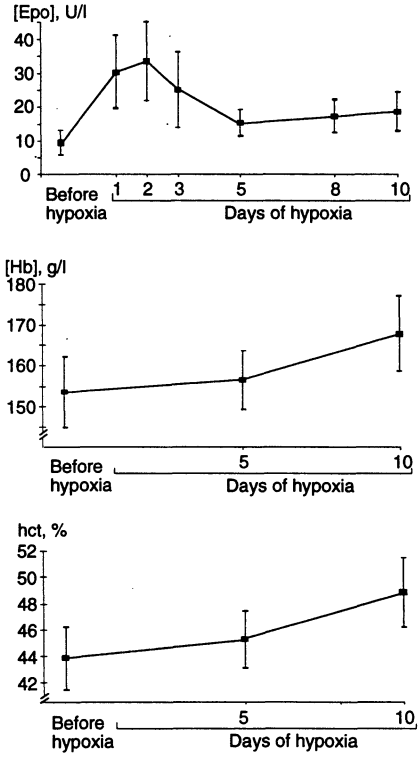
INTRODUCTION: It is well established that erythropoietin concentration ([epo]) increases in man after exposure to hypoxia. Long term studies have been performed in mountains under various uncontrolled environmental circumstances, but long term studies of [epo] under controlled conditions are lacking. Therefore, the aim of the present study was to study [epo] and some other relevant blood parameters before and during 10 days of controlled normobaric hypoxia.

MATERIAL AND METHODS: Seven healthy male volunteers aged from 20 to 23 years participated in the study. Blood samples for [epo], hemoglobin concentration ([Hb]), hematocrite (hct), and ferritin concentration ([fer]) were obtained before, and after 1, 2, 3, 5, 8 and 10 days of continuous exposure to normobaric hypoxia (14% oxygen). [Epo] was analyzed according to Wide (1990) and [Hb], hct and [fer] were analyzed by routine methods at the Karolinska hospital.

RESULTS: Erythropoietin, hemoglobin, and hematocrite concentrations (Mean±S.D.) before and during 10 days of normobaric hypoxia (14 % O_2) are presented in the figures. [Epo] increased from 9.5±3.51 U/l to 33.6±11.64 U/l ($p<.05$) after 2 days of hypoxia. Thereafter [epo] decreased to 15.4±3.92 U/l ($p<.05$) after 5 days. After 10 days [epo] was still increased (18.7 ± 5.83 U/l) as compared to before hypoxia ($p<.05$). [Hb] and hct increased over the 10 days of hypoxia [Hb] from 152±8.9 g/l to 168±9.2 g/l, and hct from 43 ± 2.4% to 49 ± 2.6%) ($p<.001$). [Fer] decreased significantly during the hypoxic exposure from 82±46.9 mmol/l to 44±31.7 mmol/l after 10 days ($p<.01$).

CONCLUSION: The initial increase of [epo] under controlled hypoxia is marked and more accentuated than in earlier data obtained during mountain sojourn at similar level of hypoxia. On the other hand, the [epo] levelled off after 5-9 days, which is similar to results obtained at previous mountain sojourns. [Hb] and hct increased as expected, most likely due to hemoconcentration. The decrease in [fer] was also expected and indicates decreased iron stores due to accelerated erytropoiesis.



Figures: Erythropoietin (Epo), Hemoglobin (Hb) and Hematocrite (hct) concentration before and during 10 days of normobaric hypoxia (14% O_2).

Mean(M) and standard deviation (SD) for physiological parameters measured during rest and during bicycle ergometry. The M and SD pertain to all test sessions within a specific P_{O_2} level (For better understanding see P_{O_2} profiles in Figure 7.).

HYPO 1			HYPO 2			HYPO 3		
P_{O_2}	Rest M (SD)	100W M (SD)	P_{O_2}	Rest M (SD)	100W M (SD)	P_{O_2}	Rest M (SD)	50W M (SD)
S_aO_2 (%)								
21, I	96 (1)	95 (1)	21, I	97 (1)	96 (1)	21, I	96 (1)	96 (1)
15, I	92 (1)	88 (3)	13, I	90 (3)	78 (5)	14	91 (1)	88 (1)
21, II	96 (1)	96 (1)	21, II	98 (1)	96 (1)	21, II	96 (1)	96 (1)
15, II	93 (1)	90 (2)	15	93 (1)	90 (1)			
21, III	97 (1)	97 (1)	13, II	90 (2)	84 (2)			
			21, III	97 (1)	96 (1)			
Pulse (BPM)								
21, I	84 (8)	117 (6)	21, I	81 (10)	123 (14)	21, I	94 (8)	102 (8)
15, I	89 (8)	126 (8)	13, I	94 (7)	140 (9)	14	95 (7)	109 (5)
21, II	87 (6)	119 (6)	21, II	82 (8)	121 (14)	21, II	87 (10)	104 (7)
15, II	91 (8)	129 (10)	15	85 (8)	128 (13)			
21, III	91 (7)	123 (10)	13, II	87 (10)	137 (8)			
			21, III	81 (8)	122 (12)			
End tidal O_2 (kPa)								
21, I	15.3 (0.4)	14.3 (1.1)	21, I	15.8 (0.9)	14.3 (0.7)	21, I	14.4 (1.8)	14.0 (1.3)
15, I	9.8 (0.5)	9.3 (1.0)	13, I	9.8 (0.5)	9.1 (0.8)	14	8.9 (0.3)	8.3 (0.3)
21, II	15.3 (0.6)	14.5 (0.8)	21, II	15.5 (0.5)	14.1 (0.4)	21, II	15.1 (0.4)	14.4 (0.5)
15, II	10.1 (0.4)	9.7 (0.8)	15	10.1 (0.4)	9.4 (0.5)			
21, III	15.2 (0.5)	14.7 (0.6)	13, II	8.0 (0.5)	7.8 (0.5)			
			21, III	16.0 (0.5)	15.0 (0.8)			
End tidal CO_2 (kPa)								
21, I	5.2 (0.4)	6.5 (0.7)	21, I	5.0 (0.6)	6.5 (0.4)	21, I	5.1 (0.5)	6.3 (0.3)
15, I	5.0 (0.3)	5.6 (0.6)	13, I	4.5 (0.4)	5.4 (0.7)	14	4.6 (0.2)	5.2 (0.3)
21, II	5.1 (0.3)	6.1 (0.5)	21, II	4.7 (0.5)	5.9 (0.5)	21, II	4.7 (0.3)	5.4 (0.3)
15, II	4.7 (0.2)	5.2 (0.5)	15	4.7 (0.3)	5.2 (0.3)			
21, III	4.9 (0.3)	5.7 (0.5)	13, II	4.5 (0.4)	4.9 (0.4)			
			21, III	4.8 (0.4)	5.8 (0.4)			
Breathing frequency (breaths/min)								
21, I	15 (2)	18 (4)	21, I	15 (4)	17 (4)	21, I	12 (2)	13 (2)
15, I	16 (2)	19 (4)	13, I	17 (4)	20 (5)	14	12 (2)	15 (2)
21, II	16 (3)	19 (3)	21, II	16 (4)	19 (4)	21, II	13 (4)	16 (4)
15, II	17 (2)	21 (4)	15	16 (3)	20 (3)			
21, III	17 (2)	21 (4)	13, II	17 (3)	21 (4)			
			21, III	16 (3)	19 (3)			
Ventilation (l/min)								
21, I			21, I	9 (3.5)	29 (4.3)	21, I	9 (1.3)	20 (3.0)
15, I			13, I	11 (2.8)	38 (7.5)	14	12 (2.3)	24 (2.9)
21, II			21, II	11 (3.9)	32 (5.5)	21, II	11 (1.1)	22 (2.5)
15, II			15	11 (2.4)	36 (3.7)			
21, III			13, II	12 (3.3)	42 (5.0)			
			21, III	10 (2.7)	31 (3.3)			
Perceived exertion								
21, I			21, I		2.9 (1.2)	21, I		
15, I		3.9 (0.9)	13, I		2.6 (1.0)	14		1.1 (0.3)
21, II		2.5 (0.8)	21, II		2.1 (0.3)	21, II		1.3 (0.7)
15, II		3.0 (0.7)	15		2.8 (0.3)			
21, III		1.9 (0.9)	13, II		3.1 (1.2)			
			21, III		2.6 (0.9)			

Mean (M) and standard deviation (SD) for measurements of hand grip strength, critical flicker fusion threshold, and optical readaptation time (RAT). The M and SD pertain to all test sessions within a specific P_{O2} level (For better understanding see P_{O2} profiles in Figure 7.).

HYPO 1 P_{O2}	M	(SD)	HYPO 2 P_{O2}	M	(SD)	HYPO 3 P_{O2}	M	(SD)
Hand grip strength, preferred hand (kp)								
			21, I	55.9	(7.9)	21, I	62.2	(8.2)
			13, I	52.8	(8.9)	14	62.8	(6.6)
			21, II	55.5	(10.1)	21, II	65.5	(7.7)
			15	54.6	(7.4)			
			13, II	53.3	(8.7)			
			21, III	55.1	(8.8)			
Hand grip strength, non preferred hand (kp)								
			21, I	53.5	(8.9)	21, I	57.6	(6.1)
			13, I	51.4	(7.3)	14	58.6	(7.7)
			21, II	52.9	(7.9)	21, II	59.3	(8.5)
			15	54.6	(10.5)			
			13, II	54.0	(11.9)			
			21, III	53.7	(12.4)			
CFF, Red								
21, I	32.8	(1.6)	21, I	32.9	(2.4)	21, I	34.7	(1.2)
15, I	33.5	(2.4)	13, I	32.9	(2.3)	14	34.1	(0.8)
21, II	34.2	(2.7)	21, II	32.7	(1.6)	21, II	34.8	(1.1)
15, II	34.3	(2.7)	15	33.2	(2.1)			
21, II	34.3	(2.3)	13, II	33.8	(2.0)			
			21, III	34.1	(2.4)			
CFF, Green								
21, I	35.3	(2.1)	21, I	35.8	(2.8)	21, I	36.8	(0.9)
15, I	36.6	(2.7)	13, I	36.1	(2.8)	14	36.4	(0.4)
21, II	37.0	(2.9)	21, II	35.5	(2.9)	21, II	36.1	(0.8)
15, II	37.3	(2.7)	15	35.6	(3.5)			
21, III	36.7	(3.4)	13, II	34.9	(1.6)			
			21, III	35.7	(3.3)			
RAT, sec								
21, I	9.8	(1.8)						
15, I	8.1	(1.4)						
21, II	7.7	(1.8)						
15, II	9.0	(1.8)						
21, III	8.8	(2.4)						

Mean(M) and standard deviation (SD) for the psychomotor tests in HYPO 2, and 3. The M and SD for the tests pertain to all test sessions within a specific P_{O2} level (For better understanding see P_{O2} profiles in Figure 7.).

HYPO 2 P_{O2}	M (SD)	X (SD)	**HYPO 3** P_{O2}	M (SD)	M (SD)
MANIKIN, response time, sec					
	sec	number of errors		sec	number of errors
21, I	2.66 (0.35)	0.7 (1.10)	21, I	2.23 (0.564)	0.7 (0.47)
13, I	2.57 (0.36)	0.8 (0.91)	14	2.18 (0.537)	0.6 (0.52)
21, II	2.41 (0.33)	0.9 (1.31)	21, II	2.13 (0.293)	0.4 (0.41)
15	2.42 (0.29)	1.1 (1.56)			
13, II	2.38 (0.22)	0.7 (0.96)			
21, III	2.35 (0.25)	0.9 (1.16)			
STROOP, response time ,sec					
Control	read word	name color		read word	name color
21, I	0.40 (0.035)	0.47 (0.045)	21, I	0.39 (0.062)	0.46 (0.063)
13, I	0.38 (0.037)	0.46 (0.057)	14	0.38 (0.060)	0.42 (0.063)
21, II	0.37 (0.032)	0.45 (0.054)	21, II	0.38 (0.065)	0.43 (0.062)
15	0.36 (0.027)	0.43 (0.046)			
13, II	0.36 (0.023)	0.42 (0.039)			
21, III	0.34 (0.024)	0.41 (0.047)			
Conflict	read word	name color		read word	name color
21, I	0.43 (0.040)	0.61 (0.094)	21, I	0.41 (0.069)	0.55 (0.098)
13, I	0.40 (0.033)	0.59 (0.091)	14	0.40 (0.071)	0.52 (0.090)
21, II	0.39 (0.029)	0.57 (0.073)	21, II	0.41 (0.087)	0.52 (0.089)
15	0.39 (0.030)	0.55 (0.075)			
13, II	0.38 (0.023)	0.51 (0.057)			
21, III	0.36 (0.021)	0.50 (0.069)			
Congruent	read word	name color		read word	name color
21, I	0.39 (0.035)	0.42 (0.052)	21, I	0.39 (0.064)	0.39 (0.052)
13, I	0.37 (0.032)	0.39 (0.054)	14	0.37 (0.064)	0.37 (0.056)
21, II	0.36 (0.036)	0.37 (0.080)	21, II	0.36 (0.050)	0.37 (0.058)
15	0.36 (0.030)	0.37 (0.052)			
13, II	0.34 (0.029)	0.36 (0.043)			
21, III	0.34 (0.024)	0.34 (0.045)			
FOUR CHOICE REACTION TIME,					
	RT	number of errors		RT	number of errors
21, I	0.32 (0.022)	8.9 (5.89)	21, I	0.32 (0.014)	10.6 (6.38)
13, I	0.31 (0.017)	7.3 (5.04)	14	0.31 (0.014)	9.4 (7.80)
21, II	0.30 (0.020)	10.0 (7.62)	21, II	0.30 (0.022)	9.4 (7.82)
15	0.30 (0.023)	10.3 (7.27)			
13, II	0.30 (0.022)	12.3 (11.09)			
21, III	0.29 (0.022)	12.8 (13.92)			
FINGER TAPPING, no. of taps with each hand					
	preferred	non-preferred		preferred	no-preferred
21, I	35 (4.3)	30 (5.0)	21, I	35 (4.7)	30 (4.2)
13, I	35 (4.2)	31 (3.4)	14	37 (4.9)	31 (5.7)
21, II	35 (5.3)	30 (4.5)	21, II	37 (4.7)	30 (6.3)
15	37 (5.5)	31 (4.3)			
13, II	37 (6.6)	31 (6.4)			
21, III	36 (5.6)	30 (5.5)			

Mean(M) and standard deviation (SD) for the Symbol coding test in HYPO 2, and 3. The M and SD for the tests pertain to all test sessions within a specific P_{O2} level (For better understanding see P_{O2} profiles in Figure 7.).

HYPO 2					HYPO 3				
P_{O2}	M	(SD)	M	(SD)	P_{O2}	M	(SD)	M	(SD)
SYMBOL CODING									
REACTION TIME, sec									
Simple rule	1 feature		2 features			1 feature		2 features	
21, I	0.61	(0.06)	0.61	(0.07)	21, I	0.57	(0.10)	0.57	(0.07)
13, I	0.58	(0.04)	0.57	(0.05)	14	0.52	(0.05)	0.51	(0.04)
21, II	0.56	(0.04)	0.57	(0.05)	21, II	0.51	(0.05)	0.50	(0.05)
15	0.56	(0.06)	0.55	(0.05)					
13, II	0.54	(0.04)	0.53	(0.04)					
21, III	0.53	(0.05)	0.54	(0.05)					
Complex rule	1 feature		2 features			1 feature		2 features	
21, I	1.35	(0.44)	1.36	(0.41)	21, I	1.16	(0.19)	1.12	(0.19)
13, I	1.24	(0.40)	1.25	(0.43)	14	0.96	(0.19)	0.94	(0.20)
21, II	1.14	(0.36)	1.10	(0.34)	21, II	0.87	(0.21)	0.89	(0.21)
15	1.08	(0.35)	1.11	(0.38)					
13, II	0.98	(0.28)	1.02	(0.29)					
21, III	0.99	(0.27)	0.99	(0.29)					
ACCURACY									
Simple rule	1 feature		2 features			1 feature		2 features	
21, I	0.98	(0.03)	0.98	(0.02)	21, I	0.96	(0.04)	0.98	(0.02)
13, I	0.97	(0.02)	0.97	(0.03)	14	0.96	(0.04)	0.96	(0.04)
21, II	0.98	(0.02)	0.97	(0.04)	21, II	0.98	(0.03)	0.95	(0.03)
15	0.96	(0.03)	0.97	(0.02)					
13, II	0.95	(0.04)	0.96	(0.05)					
21, III	0.95	(0.03)	0.95	(0.05)					
Complex rule	1 feature		2 features			1 feature		2 features	
21, I	0.97	(0.05)	0.97	(0.03)	21, I	0.94	(0.05)	0.94	(0.04)
13, I	0.98	(0.02)	0.96	(0.04)	14	0.94	(0.07)	0.95	(0.07)
21, II	0.97	(0.04)	0.97	(0.03)	21, II	0.96	(0.04)	0.96	(0.03)
15	0.97	(0.04)	0.96	(0.04)					
13, II	0.96	(0.03)	0.96	(0.03)					
21, III	0.96	(0.04)	0.95	(0.04)					

Mean(M) and standard deviation (SD) for the cognitive tests used in HYPO 1, 2, and 3. The M and SD for Ravens matrices pertain to one test session and for the other tests to all test sessions within a specific P_{O2} level (For better understanding see P_{O2} profiles in Figure 7.).

HYPO 1			**HYPO 2**			**HYPO 3**		
P_{O2}	M	(SD)	P_{O2}	M	(SD)	P_{O2}	M	(SD)
RAVEN, no. correct answers								
21, I	7.0	(1.9)	21, I	5.3	(2.3)	21, I	6.1	(1.9)
15, I	6.9	(2.0)	13, I	5.9	(1.9)	14	6.4	(1.4)
15, II	7.0	(1.6)	15	5.0	(2.8)	14	7.4	(0.8)
21, III	6.8	(2.0)	21, III	5.9	(1.4)	21, III	5.9	(1.7)
BADDELEY, efficiency								
21, I	0.71	(0.10)	21, I	0.64	(0.08)	21, I	0.71	(0.11)
15, I	0.77	(0.09)	13, I	0.67	(0.08)	14	0.78	(0.11)
21, II	0.81	(0.10)	21, II	0.67	(0.09)	21, II	0.79	(0.12)
15, II	0.83	(0.11)	15	0.69	(0.08)			
21, II	0.83	(0.09)	13, II	0.70	(0.08)			
			21, III	0.70	(0.08)			
STM, number of recalled figures								
21, I	5.1	(0.8)	21, I	4.7	(1.0)	21, I	4.7	(0.8)
15, I	5.4	(0.8)	13, I	5.3	(0.9)	14	5.3	(0.9)
21, II	5.6	(1.1)	21, II	5.0	(0.7)	21, II	5.9	(0.8)
15, II	5.7	(1.0)	15	5.4	(0.8)			
21, III	6.0	(1.1)	13, II	5.5	(1.0)			
			21, III	5.5	(0.6)			
PASAT, percent correct answers								
	n=69			n=100				
21, I	94.6	(5.7)	21, I	83.1	(11.5)			
15, I	95.5	(4.2)	13, I	85.3	(11.6)			
21, II	96.7	(4.7)	21, II	86.7	(11.1)			
15, II	97.8	(2.7)	15	90.4	(9.6)			
21, III	98.2	(2.4)	13, II	90.5	(8.0)			
			21, III	93.6	(6.3)			

Mean(M) and standard deviation (SD) for the motor tests in HYPO 2, and 3. The M and SD for the tests pertain to all test sessions within a specific P_{O2} level (For better understanding see P_{O2} profiles in Figure 7.).

HYPO 3 P_{O2}	M	(SD)	M	(SD)
MEDIUM TAPPING,				
	no. of correctly completed		no. of errors	
21, I	38	(10.7)	1.4	(2.1)
14	48	(7.4)	1.1	(1.8)
21, II	49	(12.2)	1.0	(1.1)
AIMING,				
21, I	117	(12.6)	4.2	(3.1)
14	127	(12.1)	7.0	(6.0)
21, II	127	(12.3)	10.5	(7.0)
PURSUIT AIMING,				
21, I	64	(8.0)	1.0	(1.2)
14	70	(7.0)	2.1	(2.1)
21, II	73	(8.0)	2.8	(2.3)
TRACING,				
21, I	49	(7.7)	5.1	(3.3)
14	54	(6.7)	6.4	(3.9)
21, II	57	(7.2)	6.4	(3.9)

Mean(M) and standard deviation (SD) for the different factors on the ESQ questionnaire used in HYPO 1, 2, and 3. The M and SD pertain to all test sessions within a specific P_{O2} level (For better understanding see P_{O2} profiles in Figure 7.).

HYPO 1		**HYPO 2**		**HYPO 3**	
P_{O2}	M (SD)	P_{O2}	M (SD)	P_{O2}	M (SD)
ENVIRONMENTAL SYMPTOMS QUESTIONNAIRE (ESQ)					
CEREBRAL SYMPTOMS (AMS-C)					
21, I	0.08 (0.09)	21, I	0.10 (0.21)	21, I	0.13 (0.17)
15, I	0.12 (0.14)	13, I	0.30 (0.31)	14	0.29 (0.41)
21, II	0.23 (0.32)	21, II	0.07 (0.13)	21, II	0.35 (0.50)
15, II	0.16 (0.21)	15	0.09 (0.18)		
21, III	0.10 (0.11)	13, II	0.09 (0.20)		
		21, III	0.05 (0.13)		
RESPIRATORY SYMPTOMS (AMS-C)					
21, I	0.11 (0.10)	21, I	0.24 (0.17)	21, I	0.13 (0.15)
15, I	0.22 (0.20)	13, I	0.44 (0.30)	14	0.23 (0.25)
21, II	0.23 (0.25)	21, II	0.18 (0.13)	21, II	0.32 (0.42)
15, II	0.20 (0.17)	15	0.27 (0.23)		
21, III	0.16 (0.15)	13, II	0.26 (0.19)		
		21, III	0.17 (0.12)		
EAR, NOSE, AND THROUT					
21, I	0.08 (0.11)	21, I	0.14 (0.20)	21, I	0.16 (0.27)
15, I	0.17 (0.15)	13, I	0.15 (0.19)	14	0.18 (0.33)
21,II	0.17 (0.19)	21, II	0.07 (0.12)	21, II	0.27 (0.37)
15, II	0.20 (0.22)	15	0.13 (0.13)		
21, III	0.13 (0.12)	13, II	0.10 (0.15)		
		21, III	0.10 (0.19)		
ALERTNESS					
21, I	3.13 (1.46)	21, I	4.37 (0.82)	21, I	3.97 (0.62)
15, I	3.04 (1.11)	13, I	4.05 (0.58)	14	3.99 (0.76)
21, II	2.77 (1.49)	21, II	4.47 (0.61)	21, II	3.95 (0.88)
15, II	2.80 (1.32)	15	4.37 (0.60)		
21, III	2.90 (1.22)	13, II	4.41 (0.51)		
		21, III	4.19 (0.89)		
FATIGUE					
21, I	0.45 (0.40)	21, I	0.77 (0.37)	21, I	0.46 (0.43)
15, I	0.48 (0.34)	13, I	0.90 (0.48)	14	0.78 (0.57)
21, II	0.45 (0.42)	21, II	0.67 (0.47)	21, II	0.86 (0.46)
15, II	0.48 (0.43)	15	0.80 (0.49)		
21, III	0.48 (0.39)	13, II	0.60 (0.35)		
		21, III	0.67 (0.43)		

Mean(M) and standard deviation (SD) for the factors iactivity and stress in the mood questionnaire used in HYPO 1, 2, and 3. The M and SD pertain to all test sessions within a specific P_{O2} level (For better understanding see P_{O2} profiles in Figure 7.).

HYPO 1		**HYPO 2**		**HYPO 3**	
P_{O2}	M (SD)	P_{O2}	M (SD)	P_{O2}	M (SD)
MOOD QUESTIONNAIRE					
ACTIVITY					
21, I	2.08 (0.34)	21, I	1.09 (0.64)	21, I	0.91 (0.52)
15, I	2.10 (0.29)	13, I	1.08 (0.50)	14	0.82 (0.69)
21, II	1.97 (0.37)	21, II	1.04 (0.53)	21, II	0.59 (0.36)
15, II	1.91 (0.30)	15	0.99 (0.47)		
21, III	1.94 (0.38)	13, II	1.10 (0.76)		
		21, III	1.06 (0.53)		
STRESS					
21, I	3.36 (0.27)	21, I	3.24 (0.67)	21, I	2.64 (0.79)
15, I	3.46 (0.23)	13, I	3.31 (0.71)	14	2.19 (0.97)
21, II	3.58 (0.21)	21, II	3.27 (0.75)	21, II	1.99 (0.89)
15, II	3.53 (0.22)	15	3.11 (0.78)		
21, III	3.48 (0.16)	13, II	3.07 (0.85)		
		21, III	3.25 (0.82)		

Mean(M) and standard deviation (SD) for the different factors in the Adjective questionnaire used in HYPO 3. The M and SD pertain to all test sessions within a specific P_{O2} level (For better understanding see P_{O2} profiles in Figure 7.).

HYPO 3	M (SD)	M (SD)
ADJECTIVES		
	Pre confinement	12 days confinement
Extrovertion/introversion	4.9 (0.73)	5.0 (0.60)
Aggreeableness	5.1 (0.50)	4.9 (0.53)
Conscientiousness	4.4 (0.90)	4.2 (1.29)
Neuroticism	2.9 (0.72)	2.7 (0.80)
Intellect	4.9 (0.91)	5.1 (1.02)