AETIOLOGY OF FATIGUE DURING MAXIMAL AND SUPRAMAXIMAL EXERCISE

by

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DEDICATIONS

When I embarked on this path to obtain my doctorate I had little understanding of the scale of the project that I was undertaking. The last three years of my life have been dedicated to my research culminating in this thesis and it is doubtful that I would ever have achieved it without the support and encouragement that I received from family, friends and colleagues. Although the list of people to whom I owe a debt of gratitude is long there are an outstanding few who I would like to thank personally for the significant role they have played in my life while I have been engaged with my studies. Paula, my best friend and soul mate, I marvel at the love, patience and understanding that you exhibited during the duration of my studies. Thank you for always being there through both the difficult times and the exciting times. Thank you for all the shared memories that we have and I look forward to making many more in our coming life together. Tim, as a mentor and a visionary you have inspired me with your enthusiasm and insight. Your ability to look beyond that which is taken for granted and too continuously question popular doctrine has instilled in me a desire to discover the truth. I believe that under your tutorship I am equipped to cope with any challenges that I might encounter. I cannot adequately express the gratitude I feel for the guidance you have provided me during my stay in your laboratories. Mom and dad through your constant and unconditional support you have instilled me with the self-belief that ultimately allowed me to undertake the last three years of research. I am eternally in awe of the depth of your love and commitment to your children and hope that one day I can be to my children as you have been to me. Kate and Brett, although for the last several years we have been separated by a continent you were always just a phone call away. It is rare that brothers and sisters are also such good friends. Zig and Laurie, I have valued your advice and opinions during my research. No small amount of my thesis is the result of your input. Lecturers and students in the unit, thank you all for being so accessible to discuss ideas and theories. The collective intellect of the department is evidenced throughout my thesis. Secretarial and support staff, without your behind-the-scenes work the research conducted by this unit would not be possible. Although you may at times feel unappreciated let me assure you that without your efforts it is unlikely this thesis would have been completed. For those whom I have not mentioned please know that it is not because I do not appreciate the encouragement that you have provided during the course of my thesis, but merely that I have received so much support from so many that it would require another volume to acknowledge the extent of this support. Therefore please know that you are in my thoughts and I am in your debt. Thank you once again to everyone who made this thesis possible.

DECLARATION

I, Les Nobbs,
declare that this thesis is my own unaided work, both in concept and execution, and that neither the substance nor any part of the above thesis has been submitted in the past, or is being, or is to be submitted for a degree at this University or at any other university.

Signature Signed by candidate

Date 03 March 2003

NONCLEMATURE

Abbreviation		Units
VO_2	Oxygen consumption	$L.min^{-1}$
VO_2max	Maximal oxygen consumption	$L.min^{-1}$
V_Emax	Maximal minute ventilation	$L.min^{-1}$
V_E	Minute ventilation	$L.min^{-1}$
VCO_2	Carbon dioxide production	$L.min^{-1}$
VCO_2max	Maximal carbon dioxide production	$L.min^{-1}$
RER	Respiratory exchange ratio	
FO_2	Oxygen fraction	%
F_IO_2	Inspired oxygen fraction	%
F_EO_2	Expired oxygen fraction	%
FCO_2	Carbon dioxide fraction	%
F_ICO_2	Inspired carbon dioxide fraction	%
F_ECO_2	Expired carbon dioxide fraction	%
F_IN_2	Inspired nitrogen fraction	%
PO	Power output	W
PPO	Peak power output	W
PPI	Peak power index	W
MPI	Mean power index	W
FI	Fatigue index	%
WAnT	Wingate anaerobic test	
La	Lactate	$mmol.L^{-1}$
sO_2	Oxygen saturation	%
O_2Hb	Haemoglobin saturation	%
iEMG	Integrated electromyography	mV
pO_2	Partial pressure of oxygen	mmHg
pCO_2	Partial pressure of carbon dioxide	mmHg
ATP	Adenosine triphosphate	
PCr	Phosphocreatine	
P_i	Inorganic phosphate	

ABSTRACT

The aim of this thesis was to investigate the extent of peripheral and central components in the development of fatigue during maximal exercise. Fatigue during maximal and supramaximal exercise has traditionally been modelled from the peripheral context of an inadequate capacity to supply metabolic substrate to the contracting muscles to meet the increased energy demand. However, there are a number of observations that are not compatible with the peripheral fatigue model but which support a reduced central drive during exercise acting to prevent organ failure that might occur should the work be continued at the same intensity. Candidates for the role of "exercise stopper" have been identified as mechanical forces, teleoanticipation, cardiovascular capacity and dyspnoea. We explored these various possibilities in order to determine the most likely cause of exercise cessation during high intensity exercise.

The development of a plateau in oxygen consumption during maximal incremental exercise has traditionally been used as evidence that an oxygen deficiency in the exercising muscles causes the termination of exercise. However, the incidence of this "plateau phenomenon" depends largely on mode of exercise, testing protocol and sampling frequency. The aim of this study was to examine whether the development of the "plateau phenomenon" is an artefact of pedalling cadence. In the first study nine healthy individuals performed in random order a maximal incremental ramp test (0.5 $W.s^{-1}$) on four occasions at a fixed cadence of 60, 80 or 100 rpm and at a self-selected cadence. Oxygen consumption (VO_2), CO_2 production (VCO_2), minute ventilation (V_E) and heart rate were measured throughout each trial and averaged over 30 s. Cadence was recorded every second. Neither VO_2max nor peak power output were different between trials. Submaximum VO_2, VCO_2 and V_E were not influenced by cadence.

A plateau in oxygen consumption was observed in 14% of the trials. Cadence declined significantly towards the end of the self-selected cadence trial ($p < 0.05$). This ramp protocol produces a low incidence of the "plateau phenomenon" and the measured physiological variables are unaffected by cadence. Furthermore, only one subject displayed this phenomenon on more than one occasion. This strongly suggests that the "plateau phenomenon" is an artefact of the testing protocol, although the biological variation cannot be ignored and Myers et al (1990) has recently reported how the sampling interval affects the variability of plateau in oxygen consumption. The significant fall in cadence in anticipation of exercise termination during the self-selected cadence trial indicates the presence of a neural regulation, which would lead to a "plateau phenomenon" in those cycle tests in which the work rate is cadence-dependent.

The purpose of the second study was to assess whether pacing strategies are adopted during supramaximal exercise bouts lasting longer than 30 s. Eight healthy males performed six Wingate Anaerobic Tests (WAnT). Subjects were informed that they were performing four 30 s WAnT and a 33 s and 36 s WAnT. However, they actually completed two trials of 30, 33 and 36 s each. Temporal feedback in the deception trials was manipulated so that subjects were unaware of the time discrepancy. Power output (PO) was determined from the angular displacement of the flywheel and averaged over 3 s. The peak power (PPI), mean power (MPI) and fatigue (FI) indices were calculated for each trial. Power output was similar for all trials up to 30 s. However, at 36 s the PO was significantly lower in the 36 s deception trial compared to the 36 s informed trial (392 ± 32 W vs. 470 ± 88 W) ($p < 0.001$). The MPI was significantly lower in the 36 s trials (714 ± 76 W and 713 ± 78 W) compared to the 30 s trials (745 ± 65 W and 764 ± 82 W) although they were not different at 30 s (764 ± 83 W and 755

± 79 W). The significant reduction in FI was greatest in the 36 s deception trial. In conclusion, the significant reduction in PO in the last six seconds of the 36 second deception trial, but not in the 36 second informed trial, indicates the presence of a pre-programmed 30 second "end point" based on the anticipated exercise duration from previous experience. Furthermore the similarity in pacing strategy in all informed trials suggests that the pacing strategy is centrally regulated and is independent of the total work to be performed.

Athletes adopt a pacing strategy to delay fatigue and optimise athletic performance. However, many current theories of the regulation of muscle function during exercise do not adequately explain all observed features of such pacing strategies. We studied power output, oxygen consumption and muscle recruitment strategies during successive 4km cycling time trials to determine whether alterations in muscle recruitment by the central nervous system could explain the observed pacing strategies. Seven, highly trained cyclists performed three consecutive 4 km time trial intervals, each separated by 17 minutes. Subjects were instructed to perform each trial in the fastest time possible, but were given no feedback other than distance covered. Integrated electromyography (iEMG) readings were measured at peak power output and for 90 s before the end of each trial. Subjects reach a VO_2max in each interval. Time taken to complete the first and third intervals was similar. Peak power output was highest in the first interval but average power output, oxygen consumption, heart rate and post-exercise plasma lactate concentrations were not different between intervals. Power output and iEMG activity rose similarly during the final 60 s in all intervals but were not different between trials. The similar pacing strategies in successive intervals and the parallel increase in iEMG and power output towards the end of each interval suggest that these pacing strategies could not have been controlled by peripheral mechanisms.

Rather, these findings are compatible with the action of a centrally-regulated anticipatory mechanism that alters the number of motor units that are recruited and de-recruited during exercise. The extent to which peripheral feedback influences recruitment patterns could not be determined from these experiments.

The fourth study examined whether the supplementation of inspired air with a hyperoxic mixture results in a dose-dependent increase in peak work rate and maximal oxygen consumption (VO_2max) during a ramp test to volitional exhaustion. To avoid the methodological disadvantages associated with breathing the gas mixtures from mixing bags, the trials were performed in a sealed chamber in which the oxygen fraction (F_IO_2) in the ambient air was altered and subjects were able to inhale directly from the environment. The three oxygen fractions in which the subjects exercised were 21% (room air), 35 or 60%. Arterial blood sampling occurred at rest and every 3 min during the trial. The blood was analysed for the partial pressure of oxygen (pO_2), and carbon dioxide (pCO_2); pH; oxygen saturation (sO_2); haemoglobin saturation (O_2Hb); and lactate concentrations. Expired gas and heart rate were measured continuously. Arterial sO_2 and O_2Hb were elevated in both hyperoxic conditions and did not fall throughout either trial. However in the normoxic trial sO_2 and O_2Hb declined over the duration of the trial. Lactate concentrations and pH were similar between all trials. VO_2max was significantly higher with an F_IO_2 of 35 and 60% but was not different between hyperoxic conditions. Maximal ventilation (V_Emax), carbon dioxide production (VCO_2max) and heart rate were similar for all trials. Peak power output was increased in the trained athletes in the 60% F_IO_2 trial. Since the plateau phenomenon occurred infrequently in all trial (~9%) and the effect of hyperoxia on performance was less than the changes in blood oxygen carrying capacity, we conclude that hyperoxia improved exercise

performance not solely by increasing oxygen delivery to the exercising muscles.

In order to be able to directly compare the results from studies using different equipment it is important to know the interchange ability of the results from the machines. The fifth study tested the reliability and interchangeability of the two automated metabolic gas analyser systems that would be used in this series of studies at a range of submaximal workloads. Eight highly trained cyclists performed two incremental submaximal cycle ergometer tests. For each session either a Schiller CS-200 or a Vmax Series 229 automated gas analyser was used for expired gas analysis. Data for oxygen consumption (VO_2), CO_2 production (VCO_2), minute ventilation (V_E) and respiratory exchange ration (RER) were averaged for each of the five stages (200, 250, 275, 300 and 325 W). The VO_2, V_E and RER were similar between trials at all workloads. However, VCO_2 was significantly lower in the Schiller trial at workloads above 200 W ($p < 0.05$). Although there was a significant correlation between the two automated systems for the measured parameters (VO_2 = 0.78; VCO_2 = 0.80; V_E = 0.82; RER = 0.72) ($p < 0.05$), a Bland-Altman plot revealed that the limits of agreement between the two systems were unacceptably large (VO_2 = 0.53 to 1.30 $L.min^{-1}$; VCO_2 = 0.55 to 0.64 $L.min^{-1}$; V_E = -22.3 to 30.3 $L.min^{-1}$; RER = -0.03 to 0.13). The co-efficient of variation within the analysers was insignificant for both systems. Both the systems provide reliable measures of expired gas parameters. However, care should be taken in directly comparing studies that have used the two different systems due to the poor agreement between the systems.

The factors causing the termination of maximal exercise at sea level are unknown. A widely held view is that skeletal muscle anaerobiosis consequent to an inadequate oxygen delivery to the exercising muscles

limits exercise. However, there is also evidence that respiratory muscle fatigue at the high ventilatory volumes achieved during maximal exercise could also contribute. To evaluate the separate and combined effects of O_2 delivery and respiratory muscle work on maximal exercise performance, we exercised 8 highly trained cyclists in a pressure-sealed chamber in which O_2 concentrations were manipulated and helium (He) was substituted for nitrogen in the ambient air in order to reduce the work of breathing during exercise. This system ensured that external inspiratory and expiratory resistance was minimised and identical in all experimental conditions and approximated conditions present during usual exercise. During trials with O_2 enriched ambient air the peak work rate increased (451 ± 58 W vs. 429 ± 59 W). Neither maximum nor submaximal oxygen consumption was altered in F_IO_2 of 35% (5.0 ± 0.6 l.min^{-1}) compared to 21% (4.9 ± 0.7 l.min^{-1}). Substituting helium for nitrogen had no additional effect on work (453 ± 56 W) or VO_2max (4.9 ± 0.7 l.min^{-1}) beyond those observed for the hyperoxic conditions. Although submaximum V_E was reduced with helium, $V_E$max was unchanged. Since exercise was terminated at the same peak work rate (± 5 W) in the two hyperoxic conditions we postulate that the actual work rate may be the sensed variable that determines maximal exercise performance.

The findings from these studies suggest that the maintenance of physiological homeostasis and the avoidance of organ and cellular damage are of fundamental importance during maximal exercise. This is achieved through central regulation of work output based, possibly, on afferent information from the mechanoreceptors in the exercising skeletal muscles or alternatively, the extent of motor unit recruitment during maximal exercise may be hardwired in the central nervous system in a system of feed-forward control.

REVIEW OF THE LITERATURE

The word 'fatigue' is used in everyday living to describe a range of afflictions, varying from a general state of lethargy to a specific work induced burning sensation within muscle. Physiologically, 'fatigue' describes the inability to continue functioning at a prescribed work rate (Gandevia et al, 1995; Hagberg, 1981; Hawley et al, 1997) in the presence of an increased perception of effort (Enoka et al, 1992). Fatigue is ubiquitous in everyday life, but becomes particularly marked during heavy exercise. For the purposes of this review, the term 'fatigue' will refer to the volitional cessation or reduction of external work or the inability to maintain a prescribed work rate.

The development of fatigue is characterised by an initial, disproportionate increase in the perception of effort required to maintain or increase the work output before the inability to exert the required force is experienced (Cafarelli, 1988; Garner et al, 1990; Jones et al, 1983; Matthews, 1982). The seemingly dichotomous nature of fatigue has lead scientists to describe the aetiology of fatigue in terms of peripheral and central components (Gandevia, 1992; Kent-Braun, 1999).

However, the brain did not evolve merely to register representations of the world; rather it evolved for adaptive action and behaviour. Musculoskeletal structures co-evolved with appropriate brain structures so that the complete unit functions together in an adaptive fashion (Edelman, 1989). The entire systems of muscles, joints, and proprioceptive and kinaesthetic functions plus parts of the brain evolve and function together in a unitary way (Kelso, 1995). Enoka and Stuart (1992) propose that the origin of fatigue depends on the mode of work that is being undertaken; a concept that they called task dependency. St Clair Gibson et al (2001a) used the task dependency model to examine neural control mechanisms during

different types of activities. They concluded that the force output appears to be regulated through inhibitory efferent commands in order to maintain a reserve capacity within the muscle and other organs so that there is always reserve capacity during volitional exercise. The exact mechanisms of central fatigue are unknown although there has been a great deal of interest in the role of central pathways (Davis, 1995; Newsholme et al, 1987; Newsholme et al, 1995).

Fatigue during maximal and supramaximal exercise is usually modelled from the peripheral context of an inadequate capacity to supply metabolic substrate to the contracting muscles to meet the increased energy demand. This causes contractile dysfunction that is manifest in the inability to maintain or increase work output. The central component to fatigue is generally described in terms of a reduction in the neural drive or motor command to working muscles that results in a decline in the force output (Gandevia, 2001; Kay et al, 2001; Kent-Braun, 1999; Vandewalle et al, 1991). It has been suggested that the reduced central drive during exercise may be a protective mechanism to prevent organ failure if the work was continued at the same intensity (Bigland-Ritchie et al, 1984; Noakes, 2000).

The fundamental difference between the peripheral and central theories of fatigue is that the peripheral model of fatigue assumes failure at one or more sites in the chain that initiates muscle contraction. Peripheral regulation is therefore dependent on the localised accumulation or depletion of substrates within the active muscle. Whereas the central model of fatigue is an integrated mechanism that works to preserve the integrity of the system by initiating fatigue through muscle derecruitment, based on collective feedback from the periphery, before cellular or organ failure occurs. Therefore the feedback that is assimilated by the central regulator could include chemical and mechanical as well as cognitive cues.

In order to investigate the extent of peripheral and central components in the development of fatigue, it is necessary to understand the processes that occur when the metabolic rate is increased and to examine the factors that could potentially result in fatigue. The significance of these factors is dependent on the nature of the work that is being performed. Therefore the review will focus predominantly on maximal and supramaximal exercise.

Introduction

Energy metabolism during maximal and supramaximal exercise

The hydrolysis of adenosine triphosphate (ATP) provides the immediate source of energy for muscular contraction. However, the concentration of ATP stores in the muscle are limited (~27 mmol.kg^{-1}dry muscle) (Bogdanis et al, 1996; Hultman et al, 1983). Therefore several different biochemical pathways have evolved to regenerate ATP to satisfy the increased energy requirements of the contracting muscles during exercise. During the initial stages of intense or explosive exercise, the cleaving of phosphocreatine (PCr), a high-energy phosphate stored with ATP in the muscle, provides the immediate energy (Hultman et al, 1983). However, like ATP, PCr concentrations in the muscle are very low (~75 mmol.kg^{-1}dry muscle) (Bogdanis et al, 1996), sufficient for approximately only 10 s of exercise (Sjödin, 1992). The second pathway entails the breakdown of glycogen to pyruvate and lactate through a chain of enzymatic reactions (Maughan et al, 1997). Both the phosphogenic and glycolytic processes can occur without oxygen and are therefore commonly termed anaerobic metabolism, although this is a misnomer since activity of these pathways is not dependent on an absence of oxygen. Rather the reactions occur in the absence of, that is, independent of oxygen. The final pathway for the regeneration of ATP during heavy muscular activity is oxidative metabolism, which involves the oxidation of glycogen and fat (Serresse et al, 1988).

Early researchers conceptualised the relative contribution of the different energy as a continuum based upon exercise duration (Fox et al, 1969; Fox, 1979; Matthews et al, 1971) and variations of this representation continue to be presented (Åstrand et al, 1986; McArdle et al, 1991). However, few

have considered data from recent research that provide a strong argument for the re-evaluation of early assumptions regarding the relative, temporal contributions of the different energy systems to maximal exercise.

Initial estimates of the contribution of the anaerobic or oxygen-independent components were calculated from the "oxygen debt" that was believed to accrue during intense exercise (Krogh et al, 1920; Hill et al, 1923; Margaria et al, 1933) However the accuracy of this method has been questioned (Hermansen, 1981; Saltin, 1990; Vandewalle et al, 1987) and the basis for the concept of "oxygen debt" has been challenged (Bangsbo, 1996; Graham, 1996; Medbø, 1996). Bouchard et al (1991) proposed that test protocols of varying duration be designed that would stress the capacity of individual systems, which is extremely difficult considering lactate accumulation, a marker of glycolysis, occurs within the first few seconds of exercise (Bogdanis et al, 1998; Gaitanos et al, 1993; Jacobs et al, 1983b) and it has been found that the oxidative component contributes nearly a third of the ATP produced in supramaximal exercise lasting only 30 s (Serresse et al, 1988; Withers et al, 1991). Oxidative energy metabolism depends on the supply of oxygen from the cardiopulmonary system meeting the increasing demand for oxygen from the muscles although the initial limited oxygen utilisation at the onset of exercise does not appear to be due to insufficient oxygen availability (Bangsbo et al, 2000).

Oxidative energy capacity

In the early part of the twentieth century Hill and associates (1923; 1924a; 1924b; 1925) conducted a series of studies into the relationship between work and oxygen consumption. They reported that 'oxygen intake rises ... attaining a maximum ... beyond which no bodily effort can drive it. This maximum is conditioned ... by the limitations of the circulatory-respiratory

system'. Subsequent researchers have extended this observation to infer that a plateau in cardiac output occurs prior to the termination of maximal exercise (Mitchell et al, 1958). They hypothesised that the capacity of the heart to supply the exercising muscles with oxygenated blood was the limiting factor in maximal exercise. However, recently Hochachka (1999) showed that under conditions of volitional fatigue, the exercising muscle never becomes more that ~70% deoxygenated and even at this low degree of anaerobiosis, myoglobin acts to facilitate the transfer of oxygen into the mitochondria (Wittenberg et al, 1975), maintaining the oxygenation of the muscles.

Plateau phenomenon in oxygen consumption

Based on the studies by Hill and associates, a plateau in oxygen consumption has become the criteria for identifying maximal effort and maximal oxygen uptake during progressive short duration exercise to exhaustion (Basset et al, 1997; Howley et al, 1995; Taylor et al, 1955), despite evidence that fewer than 50% of subjects exhibit this plateau phenomenon at fatigue (Froelicher et al, 1974; Niemelä et al, 1980; St Clair Gibson et al, 2001a). Moreover, in elite athletes, where it has been suggested that the incidence of a plateau is more likely to occur (Wagner, 1991; Dempsey et al, 1999) the percentage is even lower (25 – 39%) (Doherty et al, 2002) (for a more comprehensive catalogue of studies that have examined the frequency of a plateau in oxygen consumption during maximal exercise refer to Table 1) . A plateau in cardiac output is a necessary corollary to a plateau in oxygen consumption (Mitchell et al, 1958).

Recently, Noakes (1997) referred to the model of a plateau in oxygen consumption as a 'creaking edifice' and questioned this fundamental concept in exercise physiology. He argued (Noakes, 2000) that the organ

most at risk during maximal exercise is not the skeletal muscle but instead the heart, which is in the unique position of providing its own blood supply. The limited capacity of the heart to function in the absence of oxygen (Gibbs, 1978; Katz et al, 1925) and the high resting extraction from the blood (Andersen, 1968; Åstrand et al, 1986; Grover et al, 1976) make it vulnerable to inadequate perfusion and "emphasises the importance of ... the coronary blood supply of the heart" (p 165) (Hill et al, 1925) and the fact that "the ability of the heart to increase its output sufficiently to meet the needs of the brain and muscles is conditional upon an adequate supply of blood to the heart itself" (p 151) (Bainbridge, 1931). It appears that in healthy individuals the coronary flow is not compromised since there is no evidence for the occurrence of cardiac ischemia during maximal exercise (Raskoff et al, 1976). However, in their Operation Everest II study, Sutton et al (1988) reported that during maximal exercise at altitude cardiac output and heart rate were attenuated supporting the hypothesis that exercise failure occurs as a protective response to organs other than skeletal muscle (Noakes et al, 2001), and is not caused by inadequate aerobic capacity or any absolute supply or organ failure that, as discussed previously, are fundamental to the premise of peripheral fatigue.

TABLE 1

Summary of the studies that have looked at the frequency of the "plateau phenomenon" during incremental maximal exercise and the criteria on which identifying the plateau was based.

Author	Plateau	Test Protocol	Criteria	Subjects
(Armstrong et al, 1995)	35-39%	Continuous	1	18 girls & 17 boys
(Cunningham et al, 1977)	18%	Continuous	1	66 boys
(Draper et al, 1999)	20-80%	Continuous and discontinuous	2	10 males
(Duncan et al, 1997)	50-60%	Continuous and discontinuous	2	10 males
(Froelicher et al, 1974)	7-33%	Taylor, Balke & Bruce Protocols		15 males
(Myers et al, 1989)	50-100%	Ramp	3	5 males & 1 female
(Myers et al, 1990)	50%	Ramp	3	10 males
(Niemelä et al, 1980)	8-22%	Continuous	4	21 males
(Rowland, 1993)	33%	Continuous	1	6 boys & 3 girls
(Rowland et al, 1992)	33%	Continuous	5	9 boys & 6 girls

(Sheehan et al, 1987)	31-69%	Continuous	5	16 boys
(Sloniger et al, 1996)	100%	Continuous		6 males & 2 females
(St Clair Gibson et al, 1999)	30-40%	Continuous and discontinuous	1	20 males
(Taylor et al, 1955)	69-94%	Continuous	5	115 males

1 Increase in VO_2 across two workloads was less than 2.1 $mL.kg^{-1}.min^{-1}$

2 Increase in VO_2 across two workloads was less than the mean increase in VO_2 less 2 standard deviations

3 Slope of the VO_2 curve was equal to zero

4 Increase in VO_2 across three workloads were within 5%

5 Increase in VO_2 across two workloads was less than 2.1 $cc.kg^{-1}$

Despite the low concentration of ATP in the muscle, depletion of intramuscular ATP does not occur even in extreme exercising conditions and even single fibres do not experience total ATP depletion (Jansson et al, 1987), which is surprising considering that during sprint exercise the utilisation of ATP can exceed 15 mmol.kg^{-1} dry muscle.s^{-1} (Lakomy, 2000). But there are reports of ATP concentrations falling to 60% of resting levels (Bangsbo et al, 1992b; Jacobs et al, 1983a) However, measurements of fibre ATP may not reflect the local concentrations at utilisation sites, and the preferential use and depletion of compartmentalised ATP pools may be an important factor in metabolic fatigue (Korge et al, 1994). Cooke and Pate (Cooke et al, 1985) identified the ratio of ATP to adenosine diphosphate (ADP) as the important factor causing slowing of contraction velocity and reasoned that increased ADP concentrations slows the rate of ATP binding to the myosin head. This is supported by the findings of Kawai (Kawai, 1986) that ADP acts as a competitive inhibitor of ATP binding to the myosin head. However, during high intensity exercise, insufficient ADP rephosphorylation stimulates deamination of ADP to inosine monophosphate (IMP) and ammonia (NH_3), which prevents the accumulation of ADP (Sahlin et al, 1991). Therefore ADP concentration may only exert this effect at low ATP concentrations.

In contrast, intracellular stores of PCr are almost completely depleted during a 10 s bout of supramaximal exercise (Bogdanis et al, 1995; Vollestad et al, 1988), although PCr breakdown continues to regenerate ATP for another 20 s (Bogdanis et al, 1996) which may account for the rapid decline in power output during the popular Wingate Anaerobic Test (Bar-Or, 1987). Concomitant to the decline in PCr is an increase in inorganic phosphate (P_i), which at fatigue in skeletal muscle can reach

concentrations several times those at rest (Dawson et al, 1978; Dawson et al, 1980) and has also been shown to increase in ischemic cardiac muscle (Allen et al, 1985; Kammermeier et al, 1982). Inorganic phosphate is a mediator of fatigue (Cooke et al, 1988; Wilson et al, 1988) and Cooke and Pate (1985) found a large decrease in tension in the presence of a high P_i concentration in isolated contracting muscle fibres.

Although the capacity to derive energy from ATP and PCr stores is limited by the size of the intramuscular store, Medbø et al (1988) has also reported a limit in the rate of anaerobic glycolysis which can increase up to 100 times that of resting metabolism (Newsholme et al, 1973). It has been proposed that the resulting increase in H^+ disrupts the contractile mechanisms (Fitts, 1994), inhibiting muscular contraction and therefore preventing ATP concentrations from falling below critical levels at which muscular rigor would develop (Spriet et al, 1987a; Spriet et al, 1987b). The mechanism by which the pH interferes with the contraction process is likely the inhibition of pH sensitivity enzymes within the glycolytic chain and by direct action on the cross-bridge cycle that reduces the rate of ATP utilisation (Hermansen, 1981).

Increased concentrations of lactate in a vigorously contracting muscle are associated with acidosis and it is sometimes difficult to differentiate the effects of lactate from the changes in pH (Bangsbo, 1997). Early assumptions that lactate production interferes with the contractile and biochemical processes in the exercising muscle has been opposed by Busa and Nuccitelli (1984) and studies in which the pH has been held constant , suggests that lactate per se is not a cause of fatigue (Bangsbo et al, 1992a). This assertion is supported by observations from a study performed on elite rowers that constructed a lactate profile over a 2000 m time trial (Hagerman, 2000). Blood lactate concentrations reached near peak levels

within 2 min (12 – 15 mMol) and then rose very little or not at all. Yet, despite the stable blood lactate levels after the first third of the race, inhibitory fatigue signals continue to become more intense over the course of the time trial and the pace of the athletes fell progressively.

Cardiac output

The first tentative studies designed to elucidate the cardiovascular response to physical activity were conducted nearly 100 years ago (Loewy et al, 1905; Plesch, 1909). However due to methodological inadequacies, it was not until Krogh and Lindhart (1912) examined blood flow through the lungs that the first accurate measures of cardiac output during physical work were recorded. They determined that approximately 5 L of blood is circulated per minute at rest and during heavy exercise they recorded a cardiac output of more than 20 $L.min^{-1}$. In fact early researchers (Christensen et al, 1914; Douglas et al, 1922; Krogh et al, 1912) recorded cardiac output values during rest (4-6 $L.min^{-1}$) and at heavy workloads (22-28 $L.min^{-1}$) that are very similar to those reported in more recent literature (Asmussen et al, 1955; Åstrand et al, 1964; Mitchell et al, 1958). Based upon the linear relationship between cardiac output and oxygen consumption (Boothby, 1915), Hill and Lupton (1923) estimated a cardiac output in excess of 40 $L.min^{-1}$ in a elite athletes, which has since been recorded (Ekblom et al, 1968b), although these authors were unable to report a plateau in cardiac output even at maximal workloads.

Heart rate

Cardiac output can be increased by an acceleration of the heart rate or a larger stroke volume, or both although an increase in the heart rate is the main contributor to the increased cardiac output during exercise (Boothby, 1915). During incremental exercise, heart rate increases linearly (Åstrand et

al, 1964) reaching a maximum at exhaustion (Andersen, 1968). Extrinsic control of heart rate is provided by both the parasympathetic and sympathetic nervous systems (Ekblom et al, 1973; Kauf, 1926; Lin et al, 1972; Tesch, 1985) and a change in the heart rate usually involves the reciprocal action of these two divisions of the autonomic nervous system. During resting conditions, the parasympathetic system exerts the primary neural control over the heart (Ekblom et al, 1973) and Kenney (1985) observed that in trained athletes the parasympathetic outflow to the heart is increased, which may account for their lower resting heart rate (McArdle et al, 1978). Maximal heart rate is attenuated as part of an adaptive training response and therefore stroke volume is increased in trained athletes to maintain the cardiac output (Saltin, 1969).

Stroke volume

Stroke volume is regulated by two main physiologic mechanisms: preload and myocardial contractility. In 1896, Starling (1896) reported that the force of cardiac contraction increased when a stretch stimulus was applied to the cardiac muscle. This has become known as Starling's Law. Any factors that increase venous return, such as arteriolar vasodilatation, the rhythmic milking action of the muscle pump and increase in venous tone, or slow the heart rate work to enhance ventricular filling during the diastolic phase of the cardiac cycle thereby applying the stretch stimulus will increase the stroke volume. Moreover, ventricular contractility is further increased by circulating catecholamines released via the sympathetic nervous system during exercise (Sarnoff et al, 1960). Stroke volume plateaus fairly early during incremental exercise (Åstrand et al, 1964; Grimby et al, 1966). However, during conditions in which the maximum heart rate is restricted the maximal cardiac output is preserved (Ekblom et al, 1972), which indicates that stroke volume is enhanced. In fact in

endurance trained athletes, the stroke volume continues increasing during maximal exercise with no plateau (Gledhill et al, 1994). This observation in combination with the adaptive training response of the maximal heart rate suggests that the heart maintains a functional reserve capacity even during maximal exercise (Andersen, 1968).

Redistribution of cardiac output

In order to maintain exercise, the blood flow to the working muscles must be sufficient to provide adequate oxygen and substrate for oxidative metabolism, to remove metabolites and to maintain temperature homeostasis. The elevation in blood flow to active muscle at the onset of exercise is rapid and remarkable (Donald et al, 1970; Vatner et al, 1970). The redistribution of cardiac output occurs from inactive organs and tissues to the vascular bed in active muscles (Blomqvist et al, 1983; Clausen, 1976; Rowell, 1974) through which blood flow can increase over 20 fold during maximal exercise (Andersen, 1968; Asmussen et al, 1955; Finch et al, 1972). Laughlin and Armstrong (1982) also demonstrated a preferential blood flow to the Type IIa fast oxidative glycolytic fibres within a mixed muscle during intense exercise.

The locally mediated vasodilatory response to increased work is directly proportional to the increased metabolic activity (Laughlin et al, 1982). However, the capacity of the capillary bed in the muscles to accommodate blood flow (~200 $mL.100g^{-1}.min^{-1}$) exceeds the pump capacity of the heart by a factor of two (Saltin, 1985). Andersen (1968) noted that blood pressure could hardly be maintained if local needs were allowed to dominate the activity of the arteriolar resistance vessels. Therefore neural regulation of vasoconstrictor tone must also be present in the arteries that "feed" exercising muscles and increased vascular resistance may even occur in the active muscle during severe exercise (Rowell et al, 1990; Saltin, 1985).

Coronary blood flow

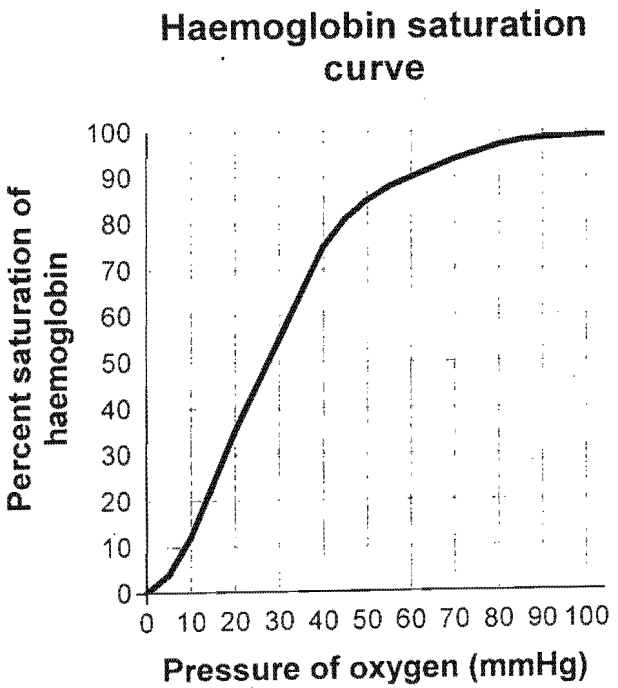
Significantly, during exercise coronary blood flow is tightly linked to the metabolic requirements (Anrep et al, 1926; Ide et al, 2000; Thomas et al, 1989). The cardiac muscle has a limited ability to function under anaerobic conditions compared to skeletal muscle (Gibbs, 1978) and even at rest the muscle extracts nearly 70% of arterial oxygen content (Feigl, 1983). With only a small increase in O_2 extraction possible during exercise, the heart is almost solely dependent on increasing coronary flow to meet the rising metabolic demands. The factor of greatest importance in the control of coronary blood flow is the pressure in the aorta (Gregg et al, 1940). The coronary arteries arise from the aorta just above the aortic valve and therefore any rise in aortic pressure is transmitted directly to the coronary arteries. The rich capillary network in the heart (Krogh, 1929; Wearn, 1928) allows for an excellent match between myocardial metabolism and coronary perfusion and there is little evidence to suggest that coronary blood flow is limited even during maximal exercise (Raskoff et al, 1976).

Pulmonary ventilation

Ambient air at sea level exerts a pressure of 760 mmHg and is composed of approximately 20.93% (159 mmHg) oxygen, 0.03% (0.2 mmHg) carbon dioxide and 79% (600 mmHg) nitrogen. As air is inspired it enters the trachea where it becomes saturated with water vapour, lowering the partial pressure of oxygen to approximately 149 mmHg. The alveolar air differs considerably from the inspired tracheal air because of the continuous exchange of oxygen and carbon dioxide between the alveoli and the blood. This exchange results in an average partial pressure for oxygen and carbon dioxide of approximately 104 mmHg and 40 mmHg, respectively (Karpovich, 1965; Matthews et al, 1976) (Figure 1). At rest the oxygen pressure in the alveolae is approximately 60 mmHg higher than the oxygen

pressure in the pulmonary capillaries thus facilitating the diffusion of oxygen through the alveolar membrane into the blood along the concentration gradient.

FIGURE 1



Blood oxygen saturation

Oxygen is transported in the blood bound to haemoglobin (Hb). The degree to which the haemoglobin is saturated by the oxygen is dependent on the partial pressure of oxygen in the blood with which it exhibits a curvilinear relationship (Barcroft, 1914; Boothby, 1915; Christensen et al, 1914) (Figure 2). This relationship is influenced by the increased CO_2 entering the lungs during exercise, which shifts the oxygen-haemoglobin association curve to the right and facilitates the diffusion of oxygen into the blood (Bohr Effect) (Barcroft, 1914). Under resting conditions, when the transit time of blood through the lungs is ~0.7 s, haemoglobin is almost completely saturated (Christensen et al, 1914) and even during maximal exercise healthy individuals are able to maintain a high level of saturation (Dempsey et al, 1980), despite an increase in flow rate of up to six times the resting value. The ability of the pulmonary capillaries to accommodate a threefold increase in the blood flow through the lungs is an important factor in maintaining the haemoglobin saturation (Dempsey, 1986). Karpovich (1965) determined that the rich perfusion of capillaries in the alveoli was analogous to the volume of blood in the lungs (~500 mL) being spread over a surface area of approximately 100 m^2 and which provided sufficient exposure to the alveolar air for gas exchange to reach an equilibrium. Furthermore, Hill et al (1925) observed that it would be futile for the heart to increase its effort if the increased blood flow resulted in arterial desaturation since arterial desaturation would result in less oxygen per volume of blood passing through the tissues. Such a scenario would negate the increase in cardiac output and put at risk the tissues that are vulnerable to ischaemia, such as the cardiac muscle itself. Hill and colleagues therefore postulated the existence of a governor that reduced the circulation rate (cardiac output) as soon as desaturation began to occur.

However, a number of authors have reported that elite athletes develop exercise-induced arterial hypoxemia during maximal (Dempsey et al, 1984) and near maximal exercise (Williams et al, 1986). Dempsey et al (1984) found that that the haemoglobin saturation in half the subjects fell below 75% during progressive maximal exercise and furthermore some subjects displayed hypoxemia during constant load exercise at 50% VO_2max. Similarly, Rice et al (1999) recently showed that trained cyclists developed exercise-induce arterial hypoxemia at 40% VO_2max. For each 1% decrement in arterial desaturation below 95% the VO_2max falls by ~2% although these impairments are reversed with breathing hyperoxic gas (Dempsey et al, 1984). The effects of maximal exercise on arterial desaturation are more pronounced in hypoxic conditions in which pulmonary oxygen diffusion is limited by the low partial pressure of oxygen in the alveoli (Hughes et al, 1968).

Hypoxia

Manipulation of the arterial oxygen saturation by ascending to altitude or breathing hypoxic gases has deleterious effects on maximal exercise performance and maximum oxygen uptake. The cardiovascular consequences of exercising at altitude is a reduction in heart rate and cardiac output at maximal workloads (Dill, 1938; Pugh, 1964; Sutton et al, 1992; Vogel et al, 1974). However, Noakes (1997) argued that the cardiovascular limitation paradigm predicts that the cardiac output should be greater than or, at the very least, equal to the cardiac output in normoxia in an effort to minimise the effects of a reduced arterial oxygen content in the blood circulating to the exercising muscles. Recently, Kayser et al (1994) observed that the electromyographic activity in the exercising muscle is reduced with increased altitude and postulated that, during exhaustive exercise at altitude the main contributor to stopping work is the

central nervous system, which reduces muscle recruitment thereby maintaining a muscle reserve and protecting the organs at risk of debilitating hypoxia (Noakes, 1988).

The earliest studies of the physiological effects of altitude were conducted at the Harvard Fatigue Laboratory by Edwards (1936) where he identified a phenomenon subsequently known as the "lactate paradox" (Hochachka et al, 2002). The lactate paradox occurs at altitude and is defined as a blood lactate concentration at fatigue that is significantly lower than the concentration found at fatigue during exercise at sea level, despite experiencing the same sensations of localised fatigue (Hochachka et al, 2002). In fact Green et al (1989) found the lactate concentration at fatigue at 8848 m was no different from resting lactate concentrations at sea level which suggests that the contracting muscles are still working aerobically at the point at which they fatigue.

Hyperoxia

It might be expected that supplementing inspired air with oxygen during exercise would result in an opposite physiological effect to that of hypoxia. However, data pertaining to the effects of an elevated inspired oxygen concentration on maximal exercise are ambiguous with improvements in performance ranging from 0 to 50% (Bannister et al, 1954; Hogan et al, 1983) and maximal oxygen consumption increases from 0 to 22% (Adams et al, 1980; Weltman et al, 1978). However, neither Ekblom et al (1975) nor Peltonen et al (2001) were able to demonstrate an increase in maximal cardiac output during exercise under hyperoxic conditions and Welch et al (1974) noted only a 6% increase in arterio-venous oxygen difference in hyperoxia, which was not sufficient to completely explain the improvement observed in VO_2max.

Further, in agreement with the above observations that the increase in VO_2max was not sufficient to explain the improvement in performance during incremental maximal exercise to exhaustion, Adams and Welch (1980) found that during high intensity exercise the performance time was improved despite no change in the VO_2. They concluded that the pH was likely the limiting factor and that the role of supplementary oxygen was related to the control of pH. Linossier (2000) similarly showed that under conditions of hyperoxia, the glycolytic processes are reduced, thereby lowering metabolic acidosis and delaying the onset of fatigue. However, they were not able to demonstrate an improved performance during an incremental maximal exercise test in hyperoxia. The inconclusive results on the effect of hyperoxia on metabolism (Hogan et al, 1983; Knight et al, 1993) has led Peltonen et al (1995) to conclude that an increase in inspired oxygen consumption must affect performance through mechanisms other than energy metabolism.

TABLE 2

Studies that have examined the effects of breathing a hyperoxic gas mixture, during exercise, on oxygen consumption, minute ventilation and performance.

Authors	Duration	Intensity	Type	F_IO_2	VO_2	V_E	Performance
(Adams et al, 1980)	10 min	55%	Constant	21 & 60%	↔	↔	
(Adams et al, 1980)	Fatigue	91%	Constant	21 & 60%	↑ 4.8%	↓	↑ 26%
(Byrnes et al, 1984)	20 min	75%	Constant	21 & 70%	↑ 13%	↓ 13%	
(Hogan et al, 1983)	Fatigue	Max	Incremental	21 & 60%	↑ 5.2%	↓ 18%	↑ 6%
(Hughson et al, 1995)	Fatigue	Max	Incremental	21 & 70%	↑ 4%		↑ 4%
(Knight et al, 1993)	Fatigue	Max	Incremental	21 & 100%	↑ 8.1%	↔	↑ 8.6%
(Peltonen et al, 1997)	2500 m	Max	Self paced	21 & 60%	↑ 11.1%	↓ 4.1%	↑ 2.2%
(Richardson et al, 1999a)	Fatigue	Max	Step increase	21 & 100%	↑ 17%		↑ 14%
(Robbins et al, 1992)	Fatigue	Max	Incremental	21 & 100%			↑ 6%

(Welch et al, 1974)	5min	95%	Constant	21 & 60%	↑ 20%	↓ 30%	
(Welch et al, 1974)	60min	65%	Constant	21 & 60%	↑ 30%	↔	
(Weltman et al, 1978)	6 min	115%	Constant	21 & 100%	↑ 22%	↓	↑ 6%
(Wilson et al, 1975)	Fatigue	110%	Constant	20 – 100%		↓	↑
(Wilson et al, 1980)	Fatigue		Constant	20 & 80%		↓ 2.2%	↑ 22%

Tissue oxygen saturation

Oxygen exerts a partial pressure of 104 mmHg in arterial blood (Matthews et al, 1976; Roca et al, 1989) and under resting conditions once the blood has passed through the active tissues, the partial pressure is reduced to 40 mmHg. However, during heavy exercise when the partial pressure of O_2 in the tissues drops below 5 mmHg (Gayeski et al, 1988) the co-efficient of utilisation (Krogh et al, 1912) can increase more than three fold (Åstrand et al, 1964) resulting in a venous oxygen partial pressure of only 20 mmHg (Roca et al, 1989). This extraction value is not uniform throughout the body however (Krogh, 1919; Uyeno et al, 1922).

The dissociation of O_2 from Hb is aided by a rightward shift in the oxygen-haemoglobin desaturation curve (Bohr Effect) (Barcroft, 1914), which is induced by the increase in partial pressure of CO_2 as well as a fall in pH and rise in temperature. These biochemical changes are all accentuated during maximal exercise. Stainsby and Otis (1964) have shown an increase in the partial pressure of CO_2 in venous blood from 40 to 90 mmHg and intramuscular pH reportedly falls as low as 6.4 following fatiguing exercise (Hermansen, 1981). The changes in these physiological variables are believed also to stimulate ventilation (Wasserman et al, 1983).

Ventilation

At rest, the ventilatory muscles use only 4% of the whole body oxygen consumption (33 $mL.L^{-1}$) (Karpovich, 1965). However during heavy exercise the energetic cost of ventilating almost 200 $L.min^{-1}$ may require more than 10% of the total oxygen uptake (~500 $mL.min^{-1}$) (Liljestrand, 1918; Nielsen, 1936; Otis, 1964). Bye et al (1983) estimated that maximal exercise that severely stresses pulmonary ventilation, the oxygen

consumption of the respiratory muscles could even reach as high as 1 $L.min^{-1}$.

Sensations of ventilatory function and the effort of breathing appear to be the only central signals that are consciously monitored during exercise (Hampson et al, 2001; Robertson, 1982). It has been noted that the changes in the sensation of pressure, volume and ventilation during exercise are promptly perceived and that peak exercise intensity coincides with peak ventilation rates (Mihevic, 1981).

The major work of breathing, particularly at higher workloads, is in overcoming the resistance in the respiratory airways. Dressendorfer et al. (1977) demonstrated that the decreased V_E, VO_2max and performance time observed during loaded breathing was reversed upon removal of the resistance. Furthermore, when the subjects exercising with the highest resistive load were given a hyperoxic gas mixture (35%), VO_2max increased significantly as did performance time, peak heart rate and expired CO_2 fraction with a slight decrease in minute ventilation. These changes suggest that the higher ambient oxygen fraction increased the oxygen saturation of the blood and therefore the oxygen availability to the exercising tissues. However, the decrease in minute ventilation indicates that exercise was not wholly limited by oxygen deficiency.

The use of demand valves to partially unload respiratory muscles during exercise has yielded ambiguous results. Harms et al (2000) observed an increase in time to exhaustion when ventilatory pressure assistance was applied. Conversely other studies have failed to find any improvements in exercise performance parameters with respiratory unloading (Gallagher et al, 1989; Marciniuk et al, 1994). However, caution should be used when interpreting these results as pressure-assisted breathing might affect performance by disrupting the natural ventilatory rhythm.

In order to avoid the obstacles associated with pressure-assisted breathing, a number of researchers have manipulated the loading associated with breathing normal air by altering the inspired gas densities (Babb, 1997b; Babb, 2001; Brice et al, 1983; Mancini et al, 1997). Flow dynamics are dependent on the velocity of flow, diameter of tubing and the density and viscosity of the inspired gas. This relationship is defined by the Reynolds number (Appendix B), which provides a threshold for turbulent flow. At rest and during low intensity exercise requiring only low tidal volumes, airflow is mostly laminar. As the velocity of flow increases in response to increasing minute ventilation, the dynamics of the air flowing through the respiratory airways changes from laminar to turbulent. The turbulence causes an increase in the resistance of flow through the respiratory pathways requiring greater muscular effort to overcome the resistance and maintain the tidal volume. Because the physical properties of helium dictate that it has a viscosity 1.76 times and a density of only 0.1 that of nitrogen, airflow of a heliox mixture becomes turbulent at a significantly higher velocity than that of air. Hence the heliox mixture reduces the work of breathing.

Bye et al (1983) highlight the development of respiratory fatigue during conditions with extreme ventilatory demands and Loke et al (1982) identified respiratory muscle fatigue in subjects who had just completed a marathon. Martin et al (1982) concluded that the decreased performance during maximal exercise was the result of ventilatory muscle fatigue brought on by isocapnic ventilation. Further support for the ventilatory limitation of exercise at high intensities is provided by the occurance of improvements in performance when subjects inspire a mixture of helium and oxygen (heliox) during exercise (Brice et al, 1983; Johnson et al, 1996; Spitler et al, 1980). The high ventilations at which these benefits occur have been used to explain the absence of significant findings in heliox

studies that utilised sub maximum workloads (Hoar et al, 1976; Spitler et al, 1980). Indeed, Cafarelli and Noble (1976) proposed that minute ventilation was related to perceived exertion only at high exercise intensities and that at lower intensities (less than 50% VO_2max), peripheral receptors in the working muscle were very likely to provide all input to effort sensation.

It has been suggested that breathing a heliox mixture during exercise might enhance performance via improved ventilatory distribution through either increased alveolar ventilation or a decrease in the alveolar-arterial oxygen difference (Glauser et al, 1969) although Nemerv et al (1983) found that physical properties of the inspired gas do not affect pulmonary gas exchange during exercise. However it must be noted that subjects in this study only exercised at 100 W, well below maximal levels.

Johnson et al (1996) credited the benefits of heliox to its ability to alter the brain's 'perception' of respiratory load and not actually prevent respiratory muscle fatigue. The effects of unloading the respiratory system can be more easily seen in patients suffering from obstructive pulmonary disorders since dyspnoea in patients with respiratory disease is the major perceptual stress experienced by the body. Although it has been demonstrated that changes in skeletal muscle enzyme activity occur in patients suffering from chronic obstructive pulmonary disease (COPD) that reduce the oxidative capacity of the peripheral muscle (Serres et al, 1998), there is evidence that COPD patients possess a skeletal muscle metabolic reserve at exhaustion (Maltais et al, 2001; Richardson et al, 1999b). This suggests that fatigue during whole body exercise in COPD patients is centrally regulated rather than the result of peripheral skeletal muscle dysfunction. The relationship between perceived respiratory effort and increased work tolerance was illustrated by an enhanced exercise time to exhaustion in COPD patients

exposed to helium or hyperoxia (Maltais et al, 2001), a finding that has been attributed to a reduction in dyspnoea at sub maximal exercise as a result of oxygen supplementation (Richardson et al, 1999b).

Interestingly, when the work of breathing was quantified in COPD patients inspiring a heliox mixture it was found that the actual work of breathing was not decreased despite the increase in the minute ventilation. This was ascribed to an increase in the minute ventilation due to the resistive unloading of the airways and the maintenance of the relationship between the work of breathing and the exercise work rate (Babb, 2001). This is borne out by further studies that failed to find a decrease in perceived breathlessness (dyspnoea) in COPD patients breathing heliox during maximal exercise (Oelberg et al, 1998; Richardson et al, 1999b). However, studies involving hypnosis have shown that the magnitude of ventilation is related to the perception of effort and not the work of exercise (Morgan et al, 1973).

Although Richardson et al (1999b) demonstrated a significant improvement in both VO_2max and peak work rates in patients with severe COPD, when exercising with heliox, this finding is not conclusive as a number of studies have failed to show any improvement in maximal work with the use of heliox in patients suffering from COPD (Babb, 2001; Oelberg et al, 1998) or cystic fibrosis (Martin et al, 1994). Inconsistencies in findings of studies looking at the effect of unloading the respiratory system through substituting helium for nitrogen have been attributed to the varying degrees of pathology, the use of different exercise modalities and methodological errors (Martin et al, 1994; Powers et al, 1986) (For a comprehensive catalogue of studies that have examined the effects of breathing a heliox mixture on exercise performance please refer to Figure

3). However, it is also possible that reducing the work of breathing may fail to alter maximal exercise performance.

TABLE 3

The effects of breathing a heliox mixture during exercise on physiological and performance parameters

Author	Comments	$\%O_2$ / %He	Delivery	VO_2	V_E	Performance
(Babb, 1997b)	Normal lung function	21/79			↑ 24%	
(Babb, 2001)	Mild COPD	21/79	Inspiratory reservoir		↑ 22%	↔
(Brice et al, 1983)		21/79	Inspiratory reservoir	↑ 4%	↑ 12-20%	
(Esposito et al, 1997)		21/79	Douglas bags	↔	↑ 12%	↔
(Esposito et al, 1997)		11/89	Douglas bags	↑ 12%	↑ 14%	↑ 15%
(Eves et al, 2001)	Full protective fire fighting gear	21/79	Self-contained breathing apparatus	↑ 10%	↑ 25%	

(Eves et al, 2001)	Full protective fire fighting gear	40/60	Self-contained breathing apparatus	↑ 22%	↑ 22%	
(Fagraeus, 1974)		21/79	Douglas bag	↑ 9%	↑ 23%	↑ 6.5%
(Powers et al, 1986)	Aerobically trained	21/79	Inspiratory reservoir	↑ 7.4%	↑ 23%	↑ 12-19%
(Wilson et al, 1980)		20/80	Inspiratory reservoir		↑ 20%	↑ 8%
(Wilson et al, 1980)		80/20	Inspiratory reservoir		↑ 1.5%	↑ 11%

Neuromuscular recruitment

In light of the constant skeletal muscular ATP concentrations that are maintained during exercise, a number of authors have begun to question the hypothesis that fatigue is caused by energy depletion (Fitts, 1994; Green, 1991) and Green (1990) has suggested that the decrease in the rate of glycolysis might be due to a reduced energy demand. There is also evidence to suggest that even in supramaximal exercise, subjects adopt a pacing strategy (Bacharach et al, 1995; Bar-Or, 1987; Katch et al, 1979) during the trial. Indirect evidence for a centrally regulated power output during supramaximal exercise bout has been provided by Vandewalle et al (1991) and Hunter et al (2003) who both observed a decline in iEMG activity over the duration of the supramaximal trial, which suggests active de-recruitment of skeletal muscle motor units. Similar falls in iEMG during an MVC have been attributed to an attempt by the central nervous system to maintain optimal force output without incurring peripheral transmission failure (Bigland-Ritchie et al, 1982; Bigland-Ritchie et al, 1983a; Bigland-Ritchie et al, 1983b).

Kayser et al (1994) studied skeletal muscle recruitment during exercise in hypoxic conditions and found that iEMG activity increased similarly in both normoxic and hypoxic conditions for upper limb exercise. However, lower limb iEMG activity did not increase during hypoxic conditions and the resultant force output in the lower limb was significantly compromised. Furthermore, when supplementary oxygen was provided in the hypoxic condition iEMG and power output both increased but remained below maximum levels reached in normoxia. This provides evidence that the total amount of muscle mass that can be recruited is regulated; in this case, through a mechanism that senses oxygen availability (Noakes et al, 2001; Peltonen et al, 2001). Even under normoxic conditions, St Clair Gibson et

al (2001b) found that cyclists recruit less than 25% of potential muscle mass during 100 km time trials. The existence of a reserve has also been described by Sloniger et al (1997) in runners. The authors found that the subjects were unable to maximally recruit their leg muscle during high intensity treadmill running bouts. They concluded that the ability to recruit additional muscle mass to meet an increased workload is limited. Richardson et al (1999b) concluded that in patients suffering from chronic obstructive pulmonary disease - where it would be expected that the availability of oxygen to working muscle is the limiting factor in exercise – fatigue occurred as a result of some form of central control rather than peripheral skeletal muscle dysfunction.

A change in the recruitment order and firing rate of motoneurones has been observed in working muscle (Bigland-Ritchie et al, 1983a). These adaptations may be force-optimising mechanisms (Bigland-Ritchie et al, 1983b) due to the slowing of contraction during intense exercise minimising the need for high, fatiguing motor neurone discharge. Afferent feedback from fatiguing muscle in particular the spindles and Golgi tendon organs (GTO) regulate the firing rates (Gandevia, 1992). This may be a model for the effects of afferent feedback to higher centres. Contrary to early reports (Merton, 1954), there is mounting evidence that muscle activation capacity declines progressively during fatiguing exercise (Gandevia et al, 1996; Kawakami et al, 2000; Loscher et al, 1996; McKenzie et al, 1992; Newham et al, 1991; Taylor et al, 2000a; Taylor et al, 2000b). Kawakami et al (2000) showed that voluntary activation of the isometric triceps surae declined from 96% to 70% during a series of 100 brief (1 s) contractions and a reduced activation (~30%) has also been reported during isokinetic contractions (Newham et al, 1991). Most of these studies involved repeated maximal voluntary contractions or maximal contractions that are maintained for over a minute. However, Loscher et al (1996)

examined a prolonged (401 ± 91 s) submaximal (30%) contraction. The imposition of a twitch interpolation just prior to volitional fatigue evoked significant increases in force output indicating that the muscle had spare capacity that was not utilised that is, the presence of a central neural regulation of force production. An electrical stimuli was applied to the triceps surae, to produce the same force, for an additional 1 min after which the subjects were able to continue the contraction voluntarily for a further 85 ± 45 s. Therefore, increased voluntary muscle activation was achievable after 1 min of electrical muscle stimulation despite the continued metabolic stress and contractile fatigue processes.

Transcranial magnetic stimulation of the cortex also increases force in supposedly maximal contractions and these increments increase in size with continuing fatigue (Gandevia et al, 1996). This suggests that the factor regulating muscle force output in these conditions is the central drive from the motor cortex. Furthermore it suggests that the corticospinal tracts and motoneurones are not acting at their limits despite maximal effort. However, the impairment in voluntary activation is sensitive to the metabolic state of the muscle because an inflated blood pressure cuff cuts off blood flow and prevents the recovery of voluntary activation that otherwise occurs within minutes of exercise (Gandevia et al, 1996). Davies and Thompson (1986) conducted a classic study where they compared the force output of a maximal voluntary contraction of the quadriceps before and after subjects ran an ultramarathon. They found that the force decreased 25% following exercise. However; a twitch interpolation returned the force output to normal. These findings provide strong evidence that the fatigue experienced after the ultramarathon was not peripherally generated but rather it was due to a decreased neural drive to the muscles.

Summary

The review of the literature reveals mechanical forces, teleoanticipation, cardiovascular capacity and dyspnoea as the most popular candidates for the role of "exercise-stopper" during maximal exercise. Most of these factors could have central or peripheral effects and the arguments for each have been explored in the review.

Purpose of the study

The present collection of studies was designed to investigate the mechanisms that regulate and limit physical work capacity during supramaximal, progressive maximal and sustained maximal exercise. In order to quantify the contribution of these potential factors in the development of fatigue during maximal exercise and the extent of the central and peripheral aspects, each factor needs to be isolated so that it can be manipulated independently and thus avoid ambiguous results. Manipulations of temporal perception, inspired oxygen concentration and inspired gas density were used to alter environmental and physiological cues that provide feedback from peripheral and sensory receptors to the central nervous system. In particular, the goal was to determine the probable relative contributions of central and peripheral mechanisms to the termination of high intensity exercise.

Materials and methods

Subjects

The subjects recruited for this research project were selected from a relatively homogenous group of trained athletes although they differed in their chosen sport. This selection was necessary to minimise the differences in physiological responses that occur between sedentary individuals and athletically active individuals. A total of 37 men volunteered to participate in the project. All the subjects were healthy at the time of the tests.

Experimental design

In studies I, IV and VI the subjects were required to perform a progressive maximal ramp test on a cycle ergometer to exhaustion under different conditions. In study I, subjects cycled at different pedalling speeds of 60, 80, 100 rpm and a self-selected cadence. During the fixed cadence trials, the pedal speed had to be maintained within 3rpm of the imposed cadence. Studies II and IV were conducted under normobaric conditions in normoxia and hyperoxia (IV), or normoxia, hyperoxia and a hyperoxic mixture of oxygen and helium (heliox) (VI). The inspired gas fractions are displayed in Table 4. The ramp protocol for the maximal tests utilised in these studies consisted of a 2 min warm-up ride at 150 W thereafter, the workload of the ramp protocol increased by 0.5 $W.s^{-1}$ until the exercise was terminated. Subjects were not informed about any physiological or performance data.

Study III used a discontinuous incremental submaximal cycle ergometer protocol. Subjects exercised for 7 min at five discrete workloads (200, 250, 275, 300 and 325 W) during which expired gas collection occurred between the 3rd and 6th minutes. The workloads were separated by 3 minutes of

light cycling (75 W). Studies I, IV-VI were all conducted on an electrically braked, cadence independent Lode cycle ergometer (Excalibur, Netherlands).

In study II, the experimental protocol consisted of six Wingate Anaerobic Tests (WAnT) each separated by a week. The trials were conducted on a Monarch friction-braked cycle ergometer (814E) and testing procedures were standardised. During the tests an onscreen counter clock provided temporal feedback. Subjects were informed that they were completing four 30 s trials, a 33 s trial and a 36 s trial. However the temporal feedback was manipulated so that they actually performed two tests for each interval. Power was recorded every 0.5 s and indices for peak power, mean power and fatigue were calculated.

In study III, the experimental protocol required the subjects to perform three consecutive 4 km performance time trials, each separated by a 17 min recovery period. Subjects were provided no performance feedback between trials except the distance remaining.

Methods used to alter gas fractions

The subjects cycled inside a Multi-place Class "A" hyperbaric chamber. For study IV the chamber was pre-filled with either room air or 35 or 60% O_2 depending on the trial to be performed. The oxygen concentration was readjusted once the subject and researcher had entered the chamber. For study VI the chamber was completely flushed through twice with the relevant mixture after the examiner and subjects had entered the chamber and the door was sealed. Once the door had been sealed, no talking was permitted in the chamber since talking would identify the presence of a helium-enriched environment. The chamber was not pressurised for any test and the F_IO_2 was continuously monitored. Typically, the percent F_IO_2

in the hyperoxic trials did not drop more than 1 - 2% throughout the duration of the trial. There were internal CO_2 scrubbers and temperature and humidity were continuously monitored.

Criteria for identifying plateau in oxygen consumption

To determine the incidence of individual plateau phenomena in the progressive maximal exercise trials (I, IV and VI), we adopted the historical methods of Taylor et al (1955). The mean increase in VO_2 across two consecutive 30 s periods from 240 s to 90 s preceding fatigue at 0 s was determined and we defined the criterion for a plateau in VO_2 in this particular testing protocol as any rate of increase in VO_2 less than 50% of the normal rate of rise in oxygen consumption. In order to avoid the error of describing a false plateau where none existed (Glassford et al, 1965), for the achievement of a true "plateau phenomenon", subjects were required to exhibit an increase in VO_2 of less than the mean increment across two consecutive 30 second periods.

Methods used to record cadence

Cadence was downloaded every second during the trial, via a RS-232 port, from the workload programmer (WLP) that was attached to the Lode cycle ergometer. The data were logged onto an excel spreadsheet. The response time from the WLP was ~30 ms. The WLP started transmission within 7 ms of receiving the request command. These values were used for time cut errors. The RS-232 signals are hard wired within the WLP and hexadecimal characters identified the request commands (Chapter 6.1).

Methods used to manipulate temporal feedback

The rate at which the on-screen counter clock displayed second intervals was manipulated through altering the firing frequency of the event that initiated incrementing the second display on the clock counter. The event frequency was changed in proportion to the altered temporal feedback (Chapter 6.2).

Measured physiological and biochemical variables

Expired respiratory gasses

In studies I, III-VI, three different automated gas analyser systems for measuring VO_2 and related parameters were used, namely the Vmax Series 229 (Sensor Medics, California) metabolic cart (I, IV and V), an Oxycon Alpha (Netherlands) (III) and the Cardiovit CS-200 (Schiller, Switzerland) Ergo-Spiro (V and VI).

In studies I, IV and V, breath-by-breath respiratory data were collected in raw data mode and VO_2, VCO_2 and RER were calculated afterwards. In studies I and IV, the data were averaged over 30 s periods to reduce breath-by-breath variability. Respiratory gases in study V and VI passed into a mixing chamber and the mean values of every 10 s were recorded. For study V, the median 13 values for each stage were averaged. For the comparison of submaximal respiratory responses during the progressive maximal trials (I, IV and VI) data were averaged forwards from the start of exercise for comparison, while for the comparison of near maximal responses the data were averaged backwards from the point of fatigue.

Haematological variables

In study VI, 4 mL of arterial blood was drawn through a cannula in the radial artery at rest, at 3 min intervals during the trial and at exhaustion for the analysis of lactate, pH and blood gasses. In study VI, 2 mL of venous blood was sampled through an antecubital cannula at similar intervals to determine plasma lactate concentrations. A 2 mL sample of venous blood was drawn in study III after the completion of each interval for lactate analysis. In study IV, partial pressure of oxygen (pO_2) and carbon dioxide (pCO_2); pH; oxygen saturation (sO_2); and haemoglobin oxygen saturation (O_2Hb) analysis was performed by a Radiometer ABL 505 (Copenhagen, Denmark) coupled to a Radiometer OSM3 (Copenhagen, Denmark). All plasma lactate concentrations were determined by spectrophotometric (Beckman Spectrophotometer – M35) enzymatic assays using a lactate kit (Lactate PAP, bioMérieux Kit, Marcey l'Etoile, France).

Heart rate

Heart rate was recorded with a Polar Accurex Plus heart rate monitor (Polar Electro.Kempele, Finland) in studies I, III, IV and VI. The data were downloaded via an interface into hrm files after completion of the trial. Maximum HR was taken as the highest HR recorded at any stage during the test.

Perceived exertion

In studies V and VI, the Borg category-ratio exertion scale was used to measure the localised effort of breathing. The category-ratio scale was selected to measure localised exertion because the growth of this scale more closely parallels the exponential increase in the ventilation during progressive exercise to exhaustion (Hassmen, 1990; Noble, 1982; Noble et

al, 1983). Furthermore, in study VI the overall level of exertion was recorded on the Borg 15-point RPE scale. No prompting was given by the researcher in translating their feeling into numerical ratings on the either scale.

Neuromuscular function

In study VI, the electromyographic (EMG) signals of the vastus lateralis was recorded using two surface EMG electrodes attached as a pair over the muscle belly with an inter-electrode distance of ~2cm (Strojnik et al, 1998). A third neutral reference electrode was placed on the tibial tuberosity. Raw EMG data were sampled at 2000Hz using MyoResearch 2.02 (Noraxon USA Inc, Scottsdale, Arizona, USA) software and a telemetric EMG system (Noraxon USA, Inc., Scottsdale, Arizona, U.S.A.). EMG data were then full-wave rectified, and smoothed root mean square. Typical noise and artefact from power lines was removed using a 60 Hz notch filter. A Butterworth six-pole filter was applied and finally the data were subjected to a bandpass filter for 10 – 200 Hz and integrated for further analysis. Electromechanical delay was treated as a systematic error, as it was assumed that this was either negligible or constant (Gollhofer et al, 1991). The integrated EMG obtained from three maximal force trials were used to normalize the EMG values of the subsequent incremental ramp cycle ergometer test.

In study III, electrodes (Thought Technology Triode™ MIEPO1-00, Montreal, Canada) with a bandwidth of 20-500 Hz and sensitivity of < 0.08 μV were attached to the rectus femoris muscle. The electrodes were linked via a fibre-optic cable to a Flexcomp/DSP EMG apparatus (Thought Technology Montreal, Canada) and host computer. The EMG signals from the electrode were band-pass filtered (20-500 Hz) and amplified using standard differential amplifiers (Thought Technology, Montreal, Canada;

common mode rejection ratio > 130 dB at 1 kHz, input impedance = 1 million MegOhms, adjustable gain up to 1600). The raw EMG signals were subsequently full wave rectified, movement artefact removed using a high-pass second order Butterworth filter with a cut off frequency of 15 Hz and then smoothed with a low-pass second-order Butterworth filter with a cut-off frequency of 5 Hz. This was performed using MATLAB™ gait analysis software. The integrated EMG data (iEMG) were used for subsequent analyses. The EMG activity coinciding with the peak torque of the second maximal isokinetic trial was used to normalise the EMG values recorded during the time trials (Hunter et al, 2002).

Maximal values of VO_2, V_E, VCO_2 and power output

The VO_2max was not influenced by cadence (Study I - 60 rpm 4.9 ± 0.4 L.min^{-1}; 80 rpm 4.7 ± 0.7 L.min^{-1}; 100 rpm 4.9 ± 0.6 L.min^{-1}; PC 4.8 ± 0.5 L.min^{-1}). During study IV VO_2max was elevated in both hyperoxic conditions compared with normoxia (21% 4.8 ± 0.5 L.min^{-1} (IV); 35% 5.2 ± 0.6 L.min^{-1} (IV); 60% 5.2 ± 0.7 L.min^{-1} (IV)). However, there was no difference between any of the inspired gas conditions in study VI (normoxia 4.9 ± 0.7 L.min^{-1} (VI); hyperoxia 5.0 ± 0.6 L.min^{-1} (VI); heliox 4.9 ± 0.7 L.min^{-1} (VI)) (Figure 2a).

Similarly maximal minute ventilation was not different for any pedalling cadence (60 rpm 129 ± 12 L.min^{-1}; 80 rpm 128 ± 20 L.min^{-1}; 100 rpm 139 ± 16 L.min^{-1}; PC 140 ± 22 L.min^{-1}) or level of F_IO_2 (Study IV -21% 160 ± 21 L.min^{-1}; 35% 162 ± 30 L.min^{-1}; 60% 154 ± 27 L.min^{-1} and Study VI- normoxia 155 ± 24 L.min^{-1}; hyperoxia 157 ± 24 L.min^{-1}; heliox 163 ± 22 L.min^{-1}) (Figure 2b).

Peak rates of CO_2 production were similar for all cadences (Study I - 60 rpm 5.7 ± 0.6 L.min^{-1}; 80 rpm 5.5 ± 0.7 L.min^{-1}; 100 rpm 5.7 ± 0.7 L.min^{-1}; PC 5.7 ± 0.7 L.min^{-1}) (Figure 2c). Due to the thermal properties of helium the non-dispersive infrared CO_2 analyser was unable to accurately measure the fraction of CO_2 in the expired air during the heliox trial. Therefore data for VCO_2 and RER were measurable only in the normoxia and hyperoxia trials. There was no difference in the peak VCO_2 between different levels of F_IO_2 (Study IV - 21% 5.9 ± 0.7 L.min^{-1}; 35% 6.1 ± 0.7

hyperoxia 5.3 ± 0.6 L.min^{-1}).

Cadence did not alter the peak power output (Study I - 60 rpm 378 ± 24 W; 80 rpm 376 ± 32 W 100 rpm 372 ± 39 W; PC 383 ± 33 W). However a greater power output was achieved in hyperoxic conditions (Study VI - hyperoxia 451 ± 58 W; heliox 453 ± 56 W) compared to exercise in normoxia (Study VI - 429 ± 59 W) (Figure 2d).

Maximal heart rates were also not influenced by cadence (Study I - 60 rpm 175 ± 5 beats.min^{-1}; 80 rpm 182 ± 8 beats.min^{-1}; 100 rpm 183 ± 10 beats.min^{-1}; PC = 184 ± 10 beats.min^{-1}) or F_IO_2 (Study IV - 21% 186 ± 6 beats.min^{-1}; 35% 190 ± 7 beats.min^{-1}; 60% 188 ± 9 beats.min^{-1} and Study VI - normoxia 180 ± 8 beats.min^{-1}; hyperoxia 189 ± 6 beats.min^{-1}; heliox = 194 ± 4 beats.min^{-1})

Figure 3 shows individual values for VO_2max, V_E and maximum power output (VI). It is noticeable that whereas maximum values for VO_2max and $V_E$max varied by 6.2 and 7.8% respectively between the heliox and hyperoxia trials, the variation in maximum power output was substantially less (1.2%). This translates to an individual variation in maximum exercise performance of approximately 5 W corresponding to a difference in exercise time of 10 s.

Plateau in oxygen consumption

In accordance with the methods employed by Taylor et al (Taylor et al, 1955), we determined that the mean increase in oxygen uptake across two consecutive 30 s periods from 240 s to 90 s preceding fatigue (0 s) was 178 mLO_2.min^{-1}, 179 mLO_2.min^{-1}, 146 mLO_2.min^{-1} in study I, VI and VI,

(Barstow et al, 1996). Therefore an increase of less that 90 mL.min^{-1} across two consecutive 30 s time periods was used as the criteria for defining a plateau in oxygen consumption. However to avoid the error of describing a plateau where none existed (Glassford et al, 1965), subjects were required to exhibit two consecutive increments in oxygen consumption of less than 90 mL.min^{-1}. Based upon these parameters the incidence of the "plateau phenomenon" in studies I, IV and VI was 17, 13 and 8.3%, respectively. Thus of 84 trials only 10 (12%) displayed a plateau phenomenon.

Cadence

The preferred cadence trial produced cadences (83.5 ± 6.4 rpm) that were significantly different from the 60 (61.8 ± 0.6 rpm; $p < 0.05$) and 100 (101.9 ± 1.0 rpm; $p < 0.05$) rpm trials (Figure 4a). The cadence in the preferred cadence trial declined significantly towards the end of the trial (Figure 4b) ($p < 0.05$) whereas by design, cadence did not fall near the end of exercise in the three fixed cadence trials (Figure 4a).

Power output

The peak power outputs, reached at 60 seconds during study III were significantly higher in the first interval (Study III - 1st 556 ± 51 W; 2nd 504 ± 44 W; 3rd 506 ± 41 W) (Figure 5a). However, the average power outputs for each interval were not different (Study III - 1st 447 ± 30 W; 2nd 425 ± 33 W; 3rd 434 ± 33 W) (Figure 5b). Nor was the time taken to complete the first interval (284 ± 8 s) and the average velocity (51 ± 1 km.h^{-1}) significantly faster than for the third interval (287 ± 9 s and 50 ± 2 km.h^{-1}) although it was faster than the second interval (290 ± 9 s and 50 ± 2 km.h^{-1}) (Figure 5c). Completion times were not different between the second and

the third interval (Figure 5c). In all trials, power output declined significantly from 60 s (Figure 5d) after which it reached a plateau. However, in the second and third intervals the initial increase in power output during the first 30 seconds of exercise was less than in the first trial. Furthermore, power output rose over the final minute of exercise in the second and third trial (Figure 5d).

In the 36 s trials (II), the power output was significantly lower at 36 s in the deception trials compared with the informed trial (Study II - 392 ± 32 W vs. 470 ± 88 W) although at 30 s and 33 s there was no difference between the trials (Figure 6).

Submaximum VO_2, VCO_2, V_E and RER

The rate of rise in oxygen consumption and heart rate in the consecutive time trials (III) was similar for all intervals and after the first minute did not increase significantly over the duration of the interval (Figure 7). The changes in VO_2, VCO_2, V_E and RER for the first 6 minutes of the incremental maximal exercise tests (I, IV and VI) are depicted in Figure 8. Thereafter there was progressive subject fallout so that continuous, complete data for all these measurements are not available. Submaximum VCO_2, and RER were not different in any of the conditions. However, VO_2 was significantly lower in study IV during the trial with F_IO_2 of 21% compared with both the 35 and 60% trials. Also V_E was lower in study VI between 270 and 360 s when subjects inspired the heliox gas mixture compared with an F_IO_2 of 21%. Figure 9 shows these same variables but in the final 360 s preceding the point of exercise termination in all 9 subjects. These data show that VO_2, VCO_2, V_E and RER in the final 360 s of the trials were not influenced by any of the interventions.

between the Schiller metabolic gas analyser used in study VI and the Vmax analyser used in study IV (Figure 10), although the VO_2 was not significantly different between the Schiller and Vmax at any workload (Table 5). The coefficient of variation was 2.4% for the Schiller and 3.1% for the Vmax.

pH and lactate

The pH decreased progressively (IV) (Figure 11a) and plasma lactate concentrations rose similarly incremental maximal exercise trials (VI) (Figure 11b). Maximum plasma lactate concentrations and pH were not different between trials. Following performance time trials (III), the post exercise plasma lactate concentrations were similar for all intervals (1st 12.7 ± 2.0 mmol.L^{-1}; 2nd 12.8 ± 2.5 mmol.L^{-1}; 3rd 14.0 ± 0.4 mmol.L^{-1}) and the concentrations were not different from those observed after the incremental maximal exercise test (14.5 ± 0.8 mmol.L^{-1}) (Figure 11c).

Blood gas analysis

Partial pressure of oxygen (pO_2)

The arterial pO_2 values were significantly different between trials at all time points, also showing a dose-dependant response to increases in F_IO_2 (Table 6). The pO_2 fell during exercise in normoxia and was also lower at fatigue than at rest during exercise in 35% O_2. In contrast, pO_2 rose throughout exercise with F_IO_2 of 60% (Table 6).

Partial pressure of carbon dioxide (pCO_2)

Arterial pCO_2 rose from rest to 3 min where after it stabilised except in F_IO_2 21% when it fell at exhaustion (Table 6). Altering the F_IO_2 did not

significantly alter the arterial pCO_2, although values at fatigue were higher at F_IO_2 of 35 and 60%.

Oxygen saturation (sO_2)

The arterial sO2 was higher at all times during exercise and at exhaustion in both hyperoxic conditions than in normoxia. Oxygen saturation decreased significantly during exercise with F_IO_2 of 21% whereas it exceeded 99% in both hyperoxic trials at both rest and throughout exercise (Table 6).

Haemoglobin saturation (O_2Hb)

Haemoglobin saturation was significantly higher in both hyperoxic trials than in normoxia. Whereas O_2Hb fell during exercise with F_IO_2 of 21%, it remained unchanged during exercise in both hyperoxic conditions (Table 6).

IEMG

During the time trials in study III, the iEMG recorded during the period of maximal power output was less than 25% of iEMG activity during the MVC (1st 24.2 ± 3.5; 2nd 21.1 ± 4.2%; 3rd 23.7 ± 3.8%). There was no difference in iEMG between intervals and iEMG remained constant over the final 90 s of each interval (Figure 12a-c). Similarly there was no difference in the iEMG between the incremental maximal trials (VI), although the iEMG in all trials increased as a function of workload (Figure 12d).

Perceived effort

The effort of breathing was not influenced by either the model of automated metabolic gas analyser used (V) (Figure 13a) or the substitution

breathing increased as a function of workload in all trials.

This series of experiments was undertaken to elucidate the mechanisms that regulate and terminate work during maximal and supramaximal exercise. To accomplish this we manipulated mechanical, temporal and environmental variables and feedback. We looked at the physiological and performance adjustments to these manipulations in an attempt to determine the nature of the mechanism that limits exercise performance.

Our first major finding was the propensity for cadence to decline towards the end of an incremental maximal test in anticipation of the termination of exercise (I). If termination of exercise had been due to the build-up of metabolites in the working muscles interfering with the contractile mechanisms, the decline in cadence in the self-selected cadence trial should have occurred only after the point of termination of the fixed cadence trials. For the reason that the ability to maintain the cadence in the fixed cadence trials indicated that contractile function was not compromised at those terminal workloads. Therefore, it seems that cadence is regulated by neural control mechanisms and that the gradual decline in cadence that begins 90 s prior to exercise termination suggests an anticipated "end point" for the exercise bout. If cadence and work output fall in anticipation of the termination of exercise, this would produce a "plateau" in oxygen consumption not necessarily related to the developments of skeletal muscle anaerobiosis.

The existence of an anticipatory control in regulating work output during a bout of exercise was evident in the divergence of power output between the informed trial and temporal deception trial, towards the end of supramaximal exercise (II). Even though subjects were consciously deceived by the visual feedback cues they received from the altered timing clock, they were able to differentiate at a subconscious level between

maintained their power output in the informed trial, while a rapid drop in the power output occurred in the same period in the deception trial. The fatigue profiles over the initial 30 s suggest that a similar pacing strategy was adopted for the different trials up to 30 s. However, the dissociation in the power output between the two 36 s trials and most notably the preservation of the power output in the 36 s informed trial supports the theory proposed by Ulmer (1996) that the metabolic cost is anticipated and regulated based, in this case, partly on the expected duration of the exercise.

Ulmer (1996) hypothesised that a "central programmer" takes cognisance of either the duration or duration and distance of the planned effort and limits muscular performance through the regulation of the metabolic cost of an activity. The existence of a central programmer that regulates exercise activity is supported by our findings that in three successive time trials separated by short rest intervals, the completion times for the first and last intervals were similar despite an absence of any performance feedback. If the pacing during the intervals had been regulated by peripheral fatigue mechanisms, then power output should have fallen progressively and irreversibly during each interval, as the "fatigue metabolites" accumulated. To compensate, electrical activity in the muscles would have increased as the central neural drive increased to increase muscle fibre recruitment in an attempt to compensate for the reduced power output of the fatiguing muscle fibres.

In contrast, the iEMG activity during the final 90 s of each interval tracked the changes in power output. The parallel relationship between power output and iEMG, along with a tendency for the power output to increase over the closing stages of the intervals indicates that fatigue was not

regulation of work output. The similar blood lactate concentrations reached at the end of the exercise intervals might indicate that the pacing strategy is based on feedback from peripheral afferents, which might also explain the attenuated maximal power output during the second and third intervals since it is unlikely that the recovery period was sufficient for the complete restoration of homeostasis. This integrated feedback mechanism would prevent the critical level of substrates or metabolites being reached (Foster et al, 1994); that is, the exercise would be regulated to ensure that homeostasis is maintained.

On the evidence of the above findings it would appear that "ultimate" fatigue does not occur often in exercising humans and that the work is regulated by neural control mechanisms, which integrate afferent feedback from as yet unidentified peripheral receptors. However the question remains: What stops maximal exercise? A number of candidates have been proposed for role of "exercise stopper" in maximal exercise. The most prominent of these are the capacity of the cardiovascular system (Basset et al, 1997; Hill et al, 1923; Taylor et al, 1955); ventilation and perfusion of arterial blood (Dempsey et al, 1984; Dempsey et al, 1999); and respiratory limitations (Dempsey, 1986; Harms et al, 2000; Johnson et al, 1996).

The first important finding with regards to identifying the "exercise stopper" was the infrequent occurrence of the plateau phenomenon during progressive maximal ramp tests. Unlike the early studies that used stepwise incremental workload protocols and which reported a high incidence of the plateau phenomenon, the exercise protocol in this series of studies (I, IV and VI) consisted of a continuous ramp protocol. An apparent result was that less than 15% of the subjects exhibited a plateau in VO_2 during the progressive exercise tests. Furthermore, no subjects consistently displayed

plateau phenomenon is merely an artefact of the testing procedure (Draper et al, 1999; Duncan et al, 1997; Froelicher et al, 1974; Roca et al, 1997) and not a necessary physiological response to maximal exercise. Therefore the original interpretation of AV Hill in which a VO_2 plateau was considered that cardinal event during maximal exercise cannot be correct. Furthermore, according to his original hypothesis the plateau in oxygen consumption resulted from a plateau in cardiac output, which caused skeletal muscle anaerobiosis and lead to a lactic acidosis that interrupted the contractile mechanisms in the working muscle resulting in a reduction in the ability to produce force. However, not only is there no evidence for a plateau in cardiac output during maximal exercise (Ekblom et al, 1968a; Ekblom et al, 1975; Peltonen et al, 2001), but two recent studies (Nielsen et al, 2001; Posterino et al, 2001) have also found that lactic acid does not inhibit contractile function and there is even evidence that suggests it may have a protective role in force maintenance during exercise (Nielsen et al, 2001). Therefore, some mechanism other than skeletal muscle anaerobiosis must be acting to terminate exercise.

Katch and Katch (1973) have previously observed this decline in cadence during incremental exercise tests and noted that in systems in which work rate is cadence-dependent, a fall in cadence will cause a proportional fall in workload. Such a scenario could conceivably result in an apparent levelling off in VO_2max as a consequence of the decline in work rate. However, in the current series of studies all the continuous ramp tests were conducted on an electro-magnetically braked cycle ergometer, which maintained a power output independent of pedalling cadence. Therefore work was not compromised by changes in cadence so that an artefactual plateau phenomenon could not occur.

inhibitor. The method used to induce hyperoxia (IV and VI) was effective in increasing arterial blood sO_2, and O_2Hb and producing a dose dependent increase in arterial pO_2 (Table 6). A number of authors have postulated that during intense exercise arterial desaturation occurs in trained athletes (Dempsey et al, 1984; Dempsey et al, 1999; Williams et al, 1986), which results in performance limitation. However, our results provide no support for the occurrence of arterial desaturation during heavy exercise. Even at fatigue under normoxic conditions, where haemoglobin saturation was significantly lower than in the hyperoxic conditions, the haemoglobin saturation nevertheless remained high at 93.7% (Table 6).

Despite high arterial saturation during normoxic conditions, submaximum and maximum VO_2 was elevated in hyperoxic conditions in study IV (Figure 2a), although there was no difference in VO_2 between the hyperoxic trials (Figure 8). However, the VCO_2 remained unaltered by hyperoxia (Figure 2c), which implies a shift in metabolism away from glycolysis towards lypolysis (Adams et al, 1986). The mechanism proposed by Wagner (1991) to explain the increased VO_2 in hyperoxia integrates the circulatory and diffusion dynamics of oxygen into the blood. He postulated that changes to the dynamic, caused by changes in the arterial saturation, increase the uptake of O_2 into the tissue. However, the physiological benefits of increasing VO_2 during submaximum exercise are difficult to understand.

But, another more plausible explanation for the increased VO_2 in hyperoxia might be measurement error. Welch and Pedersen (1981) considered this a likely factor for the large increases in O_2 uptake in hyperoxia reported in the early literature (Furasawa, 1925) and even the more modern gas analysers might not be able to measure VO_2 accurately

(Hornby et al, 1995). This rationalisation appears to be vindicated by the observation that there were no differences in submaximum VO_2 during study VI (Figure 8) in which a gas analyser different from that used in study IV was employed, although study V demonstrated that the results from the two studies cannot be directly compared (Figure 10).

Maximal workload increased in hyperoxic conditions, although the effect of hyperoxia on performance was very small and it required well-trained athletes habituated to the testing protocol to produce a consistently measurable effect. Improved performance during exercise in hyperoxic conditions has been well documented (Adams et al, 1980; Hughson et al, 1995; Knight et al, 1993; Peltonen et al, 1997; Weltman et al, 1978), although the extent of the improvements reported vary widely (Adams et al, 1980; Peltonen et al, 1997). However, the unique method of conducting the tests in a pressure-sealed hyperbaric chamber in these studies (IV and VI) allowed us to measure the direct effect of hyperoxia on performance by excluding the confounding resistive and flow variables associated with traditional gas delivery systems.

Finally, the substitution of helium for nitrogen (VI) in the hyperoxic gas mixture effected no improvement in exercise performance beyond that observed for hyperoxia alone. In addition $V_E$max was unaltered in hyperoxia or helium-enriched hyperoxia. Therefore the unloading of the respiratory system failed to improve exercise performance, which suggests that afferent feedback from the respiratory muscles during maximal exercise is not a major factor determining exercise termination. However, these findings are inconsistent with those reported by a number of other authors (Babb, 1997a; Babb, 1997b; Esposito et al, 1997; Wilson et al, 1980) who found significant increases in $V_E$max during exercise with a helium gas mixture. The major difference between those studies and this

therefore, interpret their findings in light of this methodological distinction and suggest that the effect of helium in those studies was to unload the external resistance provided by the respiratory tubing and gas mixing bags thereby allowing freer breathing during exercise. Although Dressendorfer et al (1977) has demonstrated that increasing external resistance detrimentally affected exercise performance it appears that that the sensory pathways directing this inhibitory effect on exercise are only active in persons suffering from chronic obstructive pulmonary disorders or heart failure for whom substitution of helium for nitrogen in inspired air does improve exercise performance (Mancini et al, 1997; Richardson et al, 1999b). We concur with Esposito and Ferretti (1997) that ventilatory resistance is negligible in healthy humans during exercise in normoxia.

We were surprised how small was the variation in peak work rate in hyperoxia and in hyperoxia with helium (Figure 3). The coefficient of variation within peak work rates was 1.2%, equivalent to a work rate of 5 W and exercise duration of 10 seconds. In contrast the variation in peak VO_2max was 6.2%. Thus it appears as if the peak work rate itself, acting as part of a neural reflex, was the "exercise stopper" since it is difficult to imagine any other than a neural reflex that could produce such a close matching of the peak achieved work rates in the hyperoxic and heliox conditions, in the tests conducted up to 7 days apart. Such a mechanoreceptor reflex would act similarly to the J reflex in animals, which is evoked by the activation of pulmonary C fibres and inhibits muscle contraction (Gandevia et al, 2000).

The findings from this series of studies question the conclusion that maximum exercise terminates because of skeletal muscle anaerobiosis according to the peripheral model of fatigue and suggest that AV Hill and his colleagues based their concepts on misinterpretation of data. This assertion is based upon a number of observations:

- The overall incidence of the "plateau phenomenon" was extremely low (12%) and more importantly, there was no instance when a subject consistently exhibited a plateau. Furthermore, the VO_2max values during trials when a plateau was not exhibited were higher than for those during the trials when the subjects achieved a plateau.

- Cadence declines in anticipation of the termination of exercise during freely chosen cadence trials (Figure 4). The pre-emptive reduction in cadence provides strong evidence for an altered central neural regulation of maximal exercise performance and muscle reserve at fatigue.

- Power output is maintained during exercise in which subjects are accurately informed of the duration of the exercise bout. However, in trials in which the duration of exercise is understated to subjects, there is a significant drop off in power output over the final stages of the exercise (Figure 6).

- The similar completion times for the successive intervals and the reciprocal relationship between power and iEMG activity indicate that power output was being regulated by a the recruitment of muscles fibres by the central nervous system and not by the debilitating build-up of metabolic by-products (Figure 12a-c)

increase significantly even though maximal workload was significantly higher. (Figure 2). Therefore there appears to be dissociation between oxygen uptake and workload suggesting that the body maintains a reserve even during maximal exercise.

- The tight coupling of absolute ventilation to work rate in both hyperoxia and hyperoxia with helium, the remarkable similarity (~5 W) of the higher "stopping" work rate in both hyperoxia and hyperoxia with helium and the absence of evidence that exercise terminated as a result of skeletal muscle anaerobiosis (Figure 3c).

These findings support an alternative hypothesis that afferent information from the mechanoreceptors in the exercising skeletal muscles may act as the "exercise stopper" during progressive maximal exercise to exhaustion. Or else, the extent of motor unit recruitment during maximal exercise may be hardwired in the central nervous system in a system of feed-forward control and may be influenced to only a small extent by the interventions evaluated in this trial and which increased the potential for oxygen delivery to the muscles or unloaded respiratory muscle work during progressive maximal exercise to exhaustion.

Thus these findings are more easily explained by a physiological model in which the control of exercise performance is determined centrally in the brain, specifically to ensure that maximal exercise can be performed with the maintenance of physiological homeostasis and the avoidance of damage.

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TABLE 4 (IV & VI)

Inspired ambient air gas concentrations used in studies IV and VI

	Normoxia	Hyperoxia	Heliox
Study IV	21% O_2 : 79% N_2	35% O_2 : 65% N_2 & 60% O_2 : 40% N_2	
Study VI	21% O_2 : 79% N_2	35% O_2 : 65% N_2	35% O_2 : 65% He

Comparison of VO_2 values at different workloads between the Schiller CS200 and Vmax Series automated gas analysers

	Watts	Schiller	Vmax
VO_2 ($L.min^{-1}$)	200	3.2 ± 0.3	3.4 ± 0.3
	250	3.8 ± 0.3	4.1 ± 0.5
	275	4.1 ± 0.3	4.5 ± 0.4
	300	4.3 ± 0.2	4.7 ± 0.4
	325	4.6 ± 0.2	5.3 ± 0.5

TABLE 6 (IV)

Changes in arterial pO_2, pCO_2, sO_2 and O_2Hb during maximal exercise in a sealed pressure chamber with F_IO_2 of 21, 35 or 60% O_2.

Blood Parameter		Rest	3 min	6 min	Fatigue
pO_2 (mmHg)	21%	$111 \pm 11^{b,c,d,f,g}$	$92 \pm 10^{a,f,g}$	$92 \pm 11^{a,e,g}$	$94 \pm 8^{a,f,g}$
	35%	$223 \pm 12^{d,e,g}$	$217 \pm 8^{e,g}$	$212 \pm 22^{e,g}$	$203 \pm 21^{a,e,g}$
	60%	$354 \pm 25^{b,c,d,e,f}$	$369 \pm 39^{a,e,f}$	$373 \pm 10^{a,e,f}$	$371 \pm 12^{a,e,f}$
PCO_2 (mmHg)	21%	36 ± 4	38 ± 6^{d}	36 ± 6	34 ± 5^{b}
	35%	35 ± 4^{b}	40 ± 3^{a}	37 ± 5	36 ± 4
	60%	$34 \pm 9^{b,c}$	40 ± 6^{a}	39 ± 6^{a}	38 ± 7
sO_2 (%)	21%	$98.6 \pm 0.4^{b,c,d,f,g}$	$97.3 \pm 1.3^{a,c,d,f,g}$	$96.7 \pm 1.4^{a,b,f,g}$	$96.4 \pm 1.5^{a,b,f,g}$
	35%	99.3 ± 0.2^{e}	99.2 ± 0.2^{e}	99.0 ± 0.2^{e}	98.8 ± 0.1^{e}
	60%	99.7 ± 0.1^{e}	99.5 ± 0.2^{e}	99.5 ± 0.2^{e}	99.4 ± 0.2^{e}

O_2Hb (%)	21%	$95.6 \pm 0.3^{b,c,d,f,g}$	$94.5 \pm 1.2^{a,c,d,f,g}$	$93.9 \pm 1.3^{a,b,f,g}$	$93.7 \pm 1.4^{a,b,f,g}$
	35%	96.5 ± 0.2^{e}	96.4 ± 0.2^{e}	96.3 ± 0.2^{e}	96.2 ± 0.2^{e}
	60%	96.6 ± 0.3^{e}	96.6 ± 0.2^{e}	96.6 ± 0.2^{e}	96.6 ± 0.2^{e}

Figure 2 Maximal values of power output, VO_2, V_E and VCO_2 attained during maximal exercise performed according to a ramp protocol under conditions of varying cadence and inspired ambient air gas composition.

* 21% is significantly different from 35% and 60% trials ($p < 0.05$) (IV)

γ 60% is significantly different from F_IO_2 of 21% ($p < 0.05$) (IV)

δ Normoxia is significantly different from hyperoxia and heliox trials ($p < 0.05$) (VI)

Figure 3 Comparison of individual peak power output, VO_2 and V_E for each subject during maximal exercise in a sealed pressure chamber under normoxic (■), hyperoxic (▩) and heliox (□) conditions.

Figure 4 Comparison of cadence for the final 330 s of progressive maximal exercise performed according to a ramp protocol at 60 (●), 80 (□), 100 (×) rpm and a self-selected (◇) cadence.

Figure 5 Peak power and mean power output, performance time and power output profile for three consecutive 4 km time trials.

λ 1st interval is significantly different from the 2nd and 3rd intervals ($p < 0.05$) (III)

* 2nd interval is significantly different from the 1st interval ($p < 0.05$) (III)

a 1st interval is significantly different from the 2nd and 3rd intervals ($p < 0.05$) (III)

b Significantly different from 60 s in the 1st interval ($p < 0.05$) (III)

c Significantly different from 60 s in the 1st and 2nd intervals ($p < 0.05$) (III)

d Significantly different from 60 s for all intervals ($p < 0.05$) (III)

e Significantly different from the 2nd interval ($p < 0.05$) (III)

Figure 6 Comparison of power output profile for the two 30 s, 33 s and 36 s Wingate Anaerobic Tests.

* Deception trial is significantly different from informed trial ($p < 0.05$) (II)

Figure 7 VO_2 and heart rate for the duration of each of the three consecutive 4 km time trials.

Figure 8 Submaximum VO_2, V_E, and VCO_2 for the initial 360 s of progressive maximal exercise performed according to a ramp protocol under conditions of varying cadence and inspired ambient air gas composition.

* 21% is significantly different from 35% and 60% trials ($p < 0.05$) (IV)

λ 21% is significantly different from 35% ($p < 0.05$) (IV)

Figure 9 VO_2, V_E, and VCO_2 for the final 330 s of progressive maximal exercise performed according to a ramp protocol under conditions of varying cadence and inspired ambient air gas composition.

Figure 10 Bland-Altman plot depicting calculated bias and individual differences (mean ± SD) in VO_2 between Schiller and Vmax automated metabolic gas analysers.

Figure 11 Arterial pH and plasma lactate profiles for progressive exercise performed according to a ramp protocol under conditions of varying cadence and inspired ambient air gas composition and the fatigue plasma lactate concentrations following and maximal incremental step test to exhaustion and three consecutive 4 km time trials.

Figure 12 Relative iEMG (—) and power output (···) at 60, 210, 240, 270 and 300 s in each of the three consecutive 4 km time trials and the iEMG during maximal exercise in a sealed pressure chamber performed under normoxic (•), hyperoxic (x) and heliox (O) conditions.

Figure 13 Comparison of RPE at 200, 250, 275, 300 and 325 W between the Schiller CS-200 (—) and Vmax Series 229 (···) and submaximal RPE during maximal exercise in a sealed pressure chamber performed under normoxic (•), hyperoxic (x) and heliox (O) conditions.

FIGURE 2

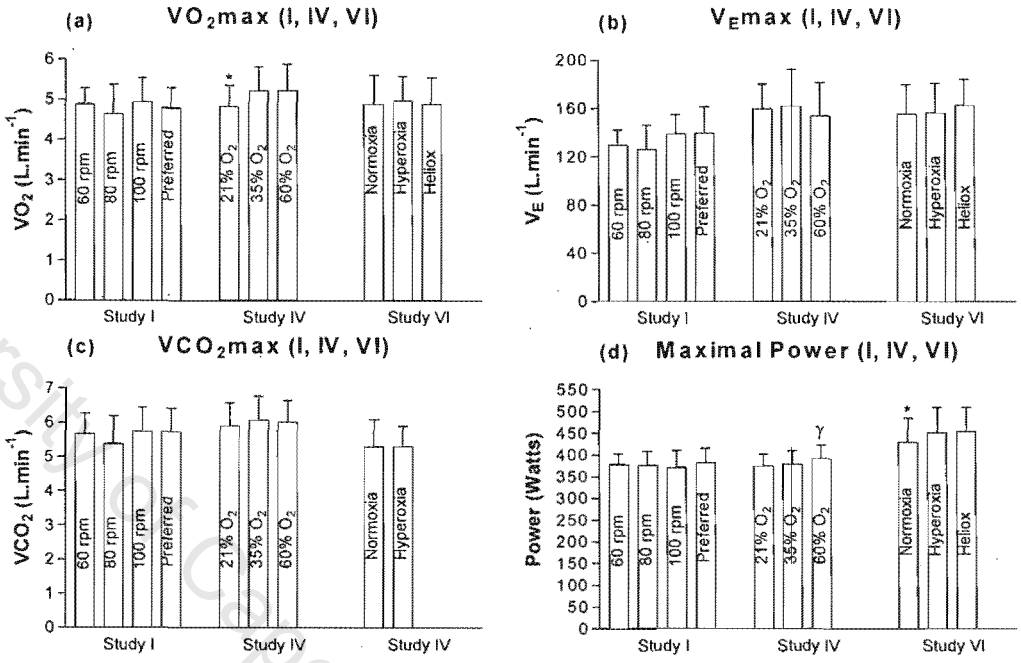
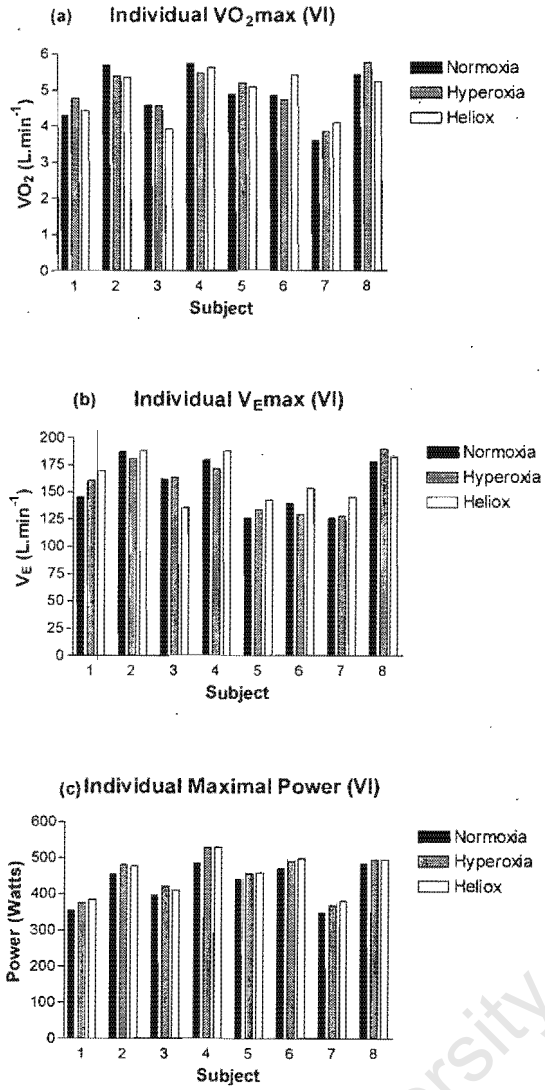
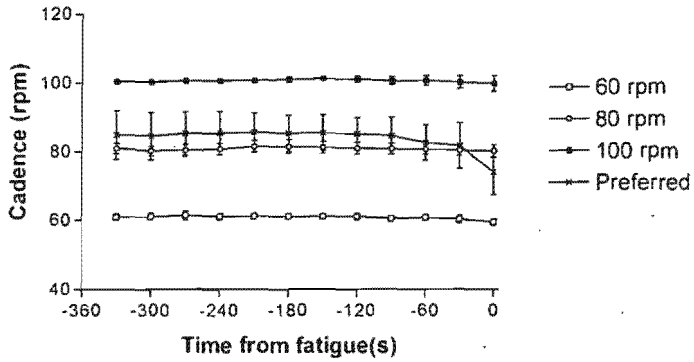


FIGURE 5



(a) Mean cadence (l)



(b) Preferred cadence (l)

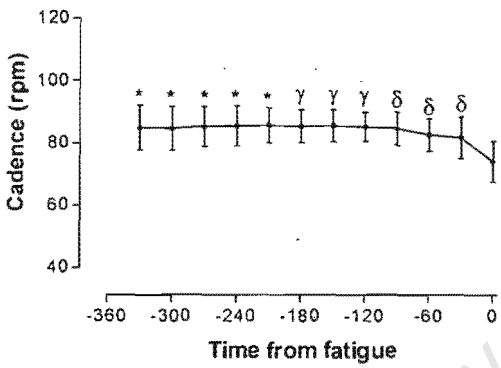
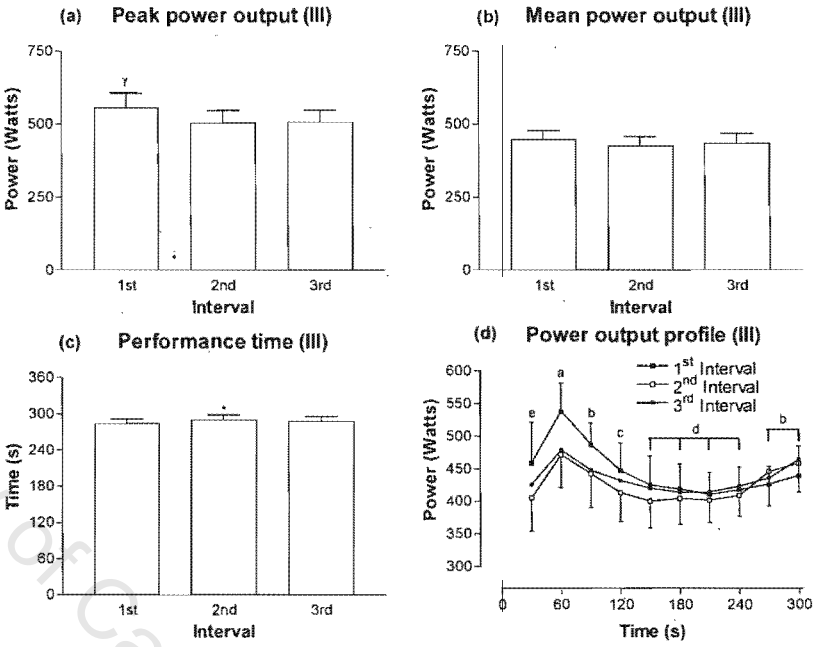
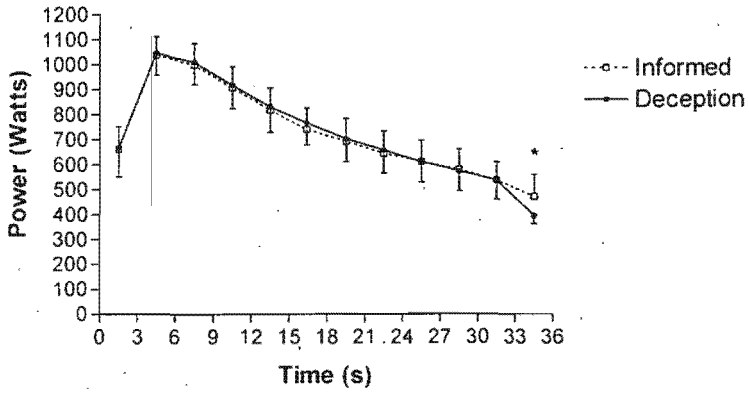


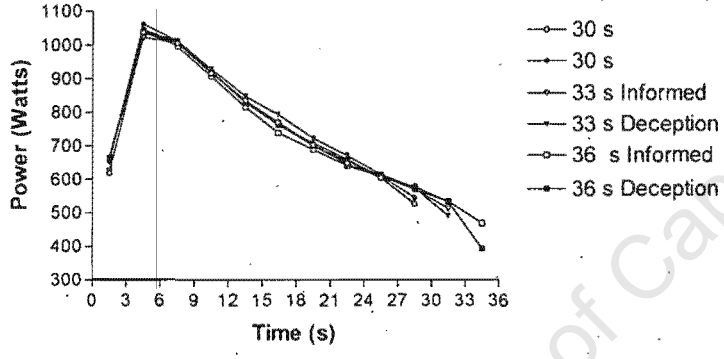
FIGURE 5

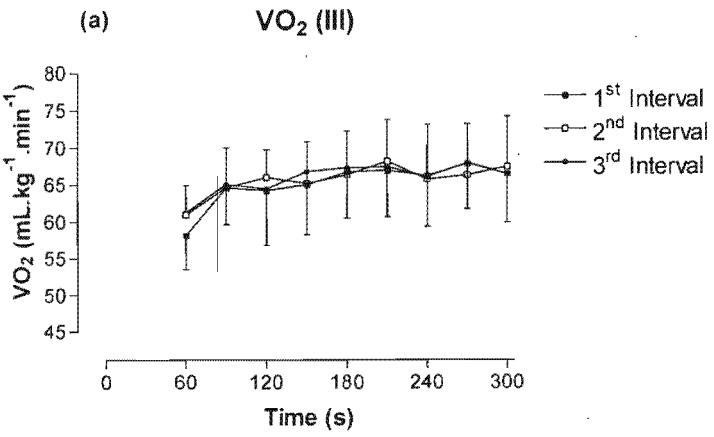


(a) Power output profile (II)



(b) Power output profile (II)





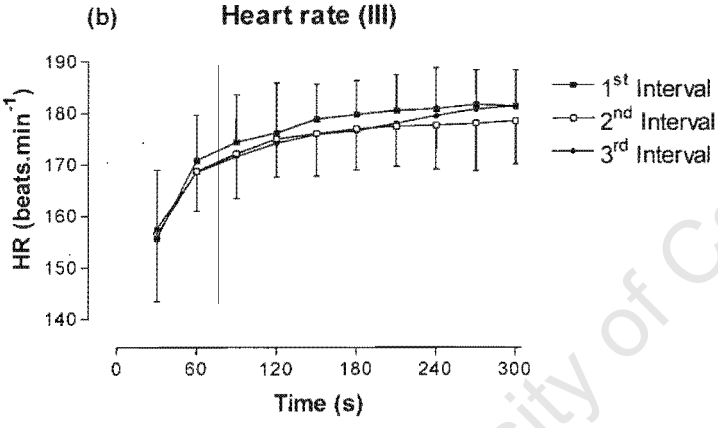


FIGURE 8

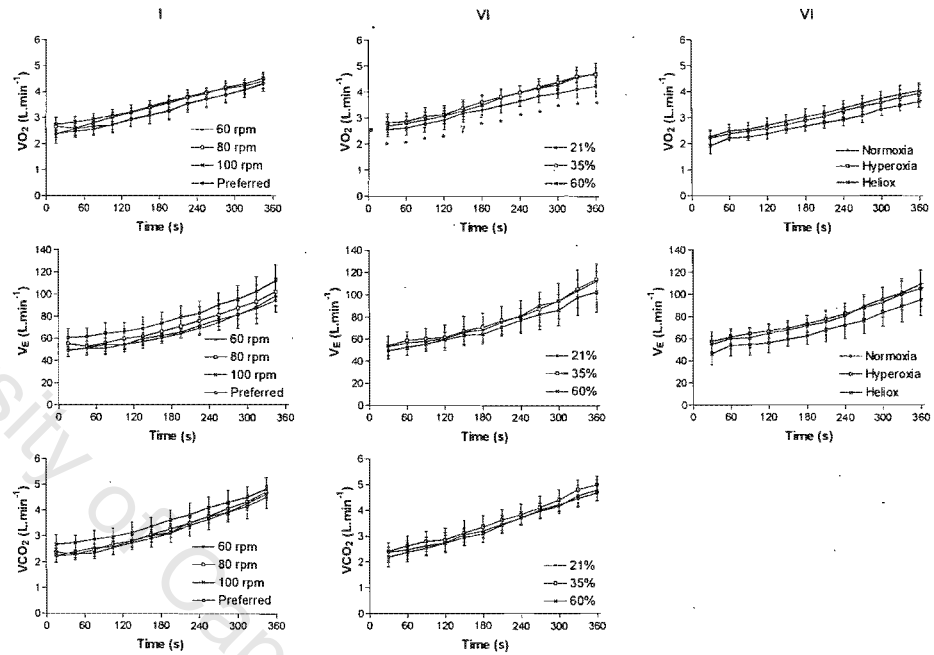


FIGURE 9

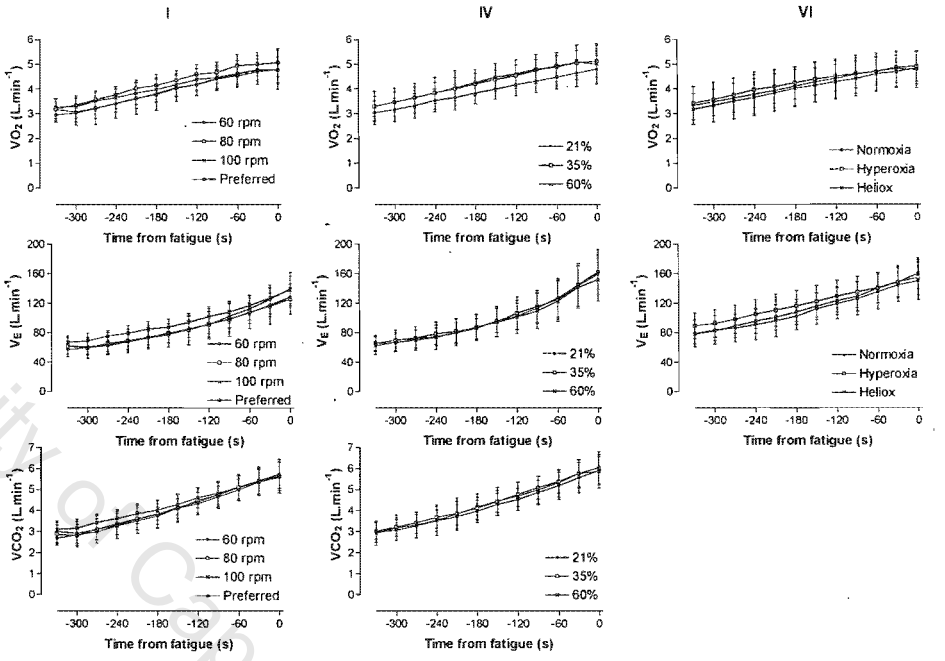


FIGURE 10

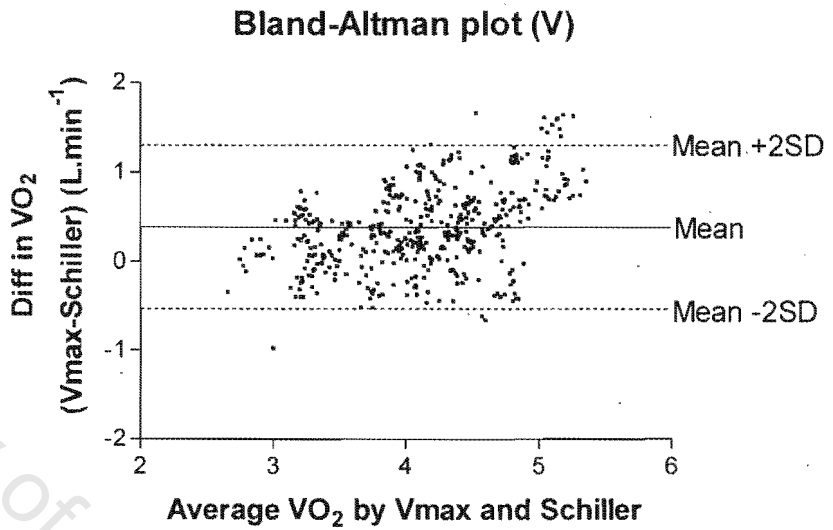
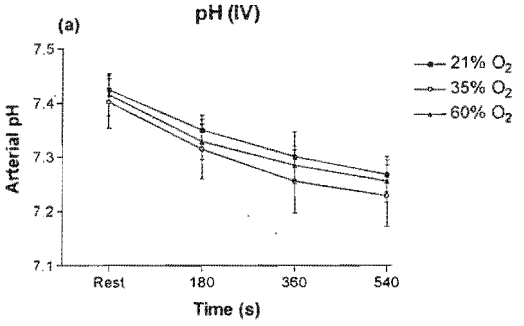
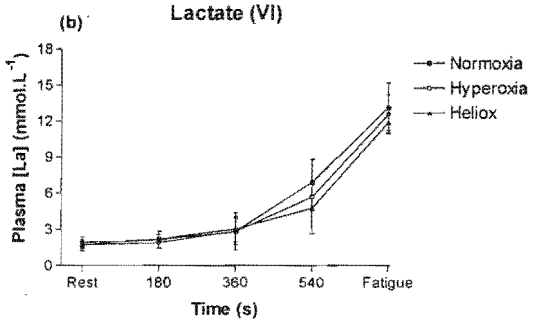


FIGURE 11





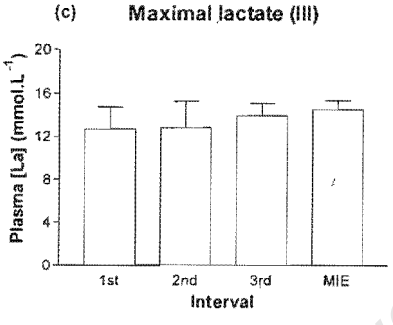
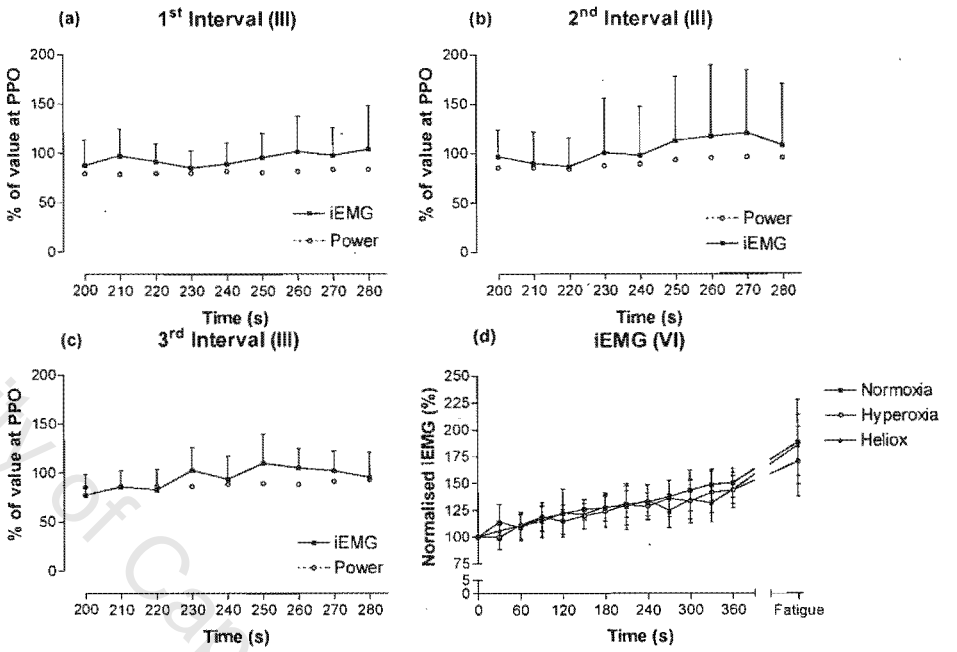
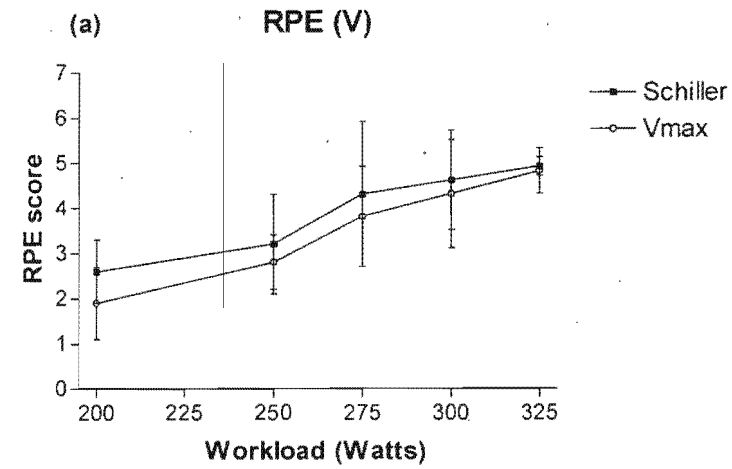
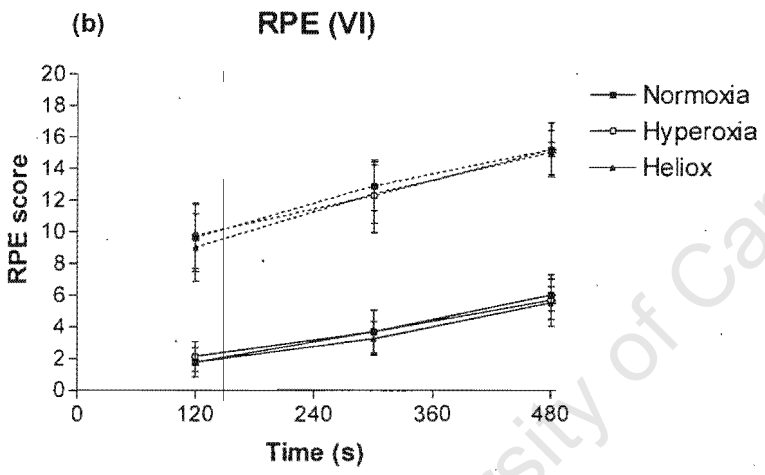


FIGURE 12







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All software applications for this project were programmed in Visual Basic programming language, which is a graphical descendant of BASIC (Beginner's All-Purpose Symbolic Instruction Code). Visual Basic is a Rapid Application Development (RAD) tool that allows individuals to write customised Windows® based compute programs.

Executable versions of these applications can be downloaded from http://www.lesnobbs.com/phd.html

Cadence capture and logging

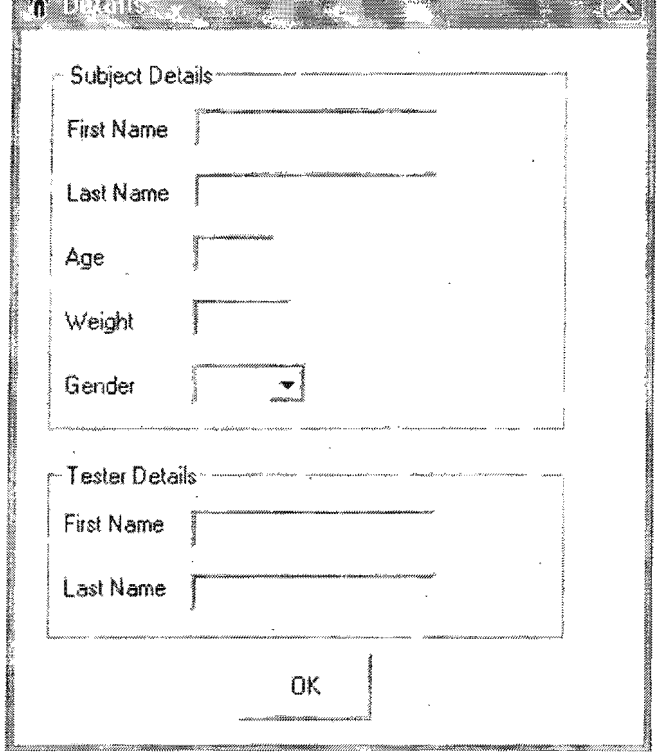
MODULE

MODLODE

```
Public modMode As Integer
Public strCadence As String
Public strLoad As String
Public strMETS As String
Public strWork As String
Public strVO2 As String
Public strClientLast As String
Public strClientFirst As String
Public strAge As String
Public strWeight As String
Public strGender As String
Public strTesterLast As String
Public strTesterFirst As String
Public blnDetails As Boolean
```

FORMS

FRMDETAILS



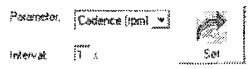

```
Option Explicit
```

```
Private Sub cmdOK_Click()
  blnDetails = True
  strClientFirst = txtFirstName.Text
  strClientLast = txtLastName.Text
  strAge = txtAge.Text
  strWeight = txtWeight.Text
  strGender = cmbGender.Text
  strTesterFirst = txtTestFirst.Text
  strTesterLast = txtTestLast.Text
  Unload Me
End Sub
```

```
Private Sub Form_Load()
  Me.Top = 700
  Me.Left = 700
  cmbGender.AddItem ("Male")
```

```
  blnDetails = False
End Sub
```

FRMWLP



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```
Option Explicit
Dim strParam As String
Dim intInterval As Integer
Dim strCommand As String
Dim strFileName As String
Dim objExcel As Excel.Application
Dim blnExcel As Boolean
Dim sCell As Single
Dim intTime As Integer
Dim strInput As String
Dim strStart As String
Dim strFinish As String
Dim blnStart As Boolean
```

```
Private Sub cmdCancel_Click()
  Dim intDay As Integer
  Dim intHour As Integer
  Dim intLenTime As Integer
  'RETRIEVE THE HOUR
  intHour = Hour(Now)
  'CHECK WHETHER A 12 OR 24 HOUR CLOCK
  Select Case intHour
    Case Is < 13
      'CHECK THAT IT IS AM
      intDay = Day(Now + 0.5)
      'IF IT IS PM ON A 12 HOUR CLOCK CONVERT TO 24 HOUR
      If intDay > Day(Now) Then
        intHour = intHour + 12
      End If
  End Select
  'FORMAT THE CURRENT TIME
  strFinish = intHour & ":" & Minute(Now) & ":" & Second(Now)
  objExcel.ActiveSheet.Cells(2, 4).Value = strFinish
  'CONVERT THE TIME INTO SECONDS
  strFinish = Val(Left$(strFinish, 2)) * 3600 +
Val(Mid$(strFinish, 4, 2)) * 60 + Val(Right$(strFinish, 2))
  'INPUT A FORMULA TO CALCULATE ELAPSED TIME
  objExcel.Cells(3, 4).Value = "= " & strFinish & " - " &
strStart
  blnStart = False
  cmdOK.Enabled = True
  cmdOK.Caption = "Re-start"
  cmdReset.Enabled = True
  cmdCancel.Enabled = False
  cmdCancel.Visible = False
  cmdSave.Visible = True
End Sub
-------------------------------------------------------------------
Private Sub cmdOK_Click()
  Dim sCounter As Single
  Dim intHour As Integer
  Dim intDay As Integer
  blnOverwrite = True
  'FIND OUT WHETHER IT IS A RESTART
  If cmdOK.Caption = "Re-start" Then
    'ASK WHETHER THE USER WANT DATA OVERWRITTEN
```

```
    End If
    If blnOverwrite = True Then
      'DELETE THE FIRST FIVE COLUMNS
      objExcel.ActiveSheet.Columns("A:E").Select
      Selection.Delete Shift:=xlLeft
      'WRITE DETAILS DATA
      Initial_Excel
      'RETRIEVE THE HOUR
      intHour = Hour(Now)
      Select Case intHour
        Case Is < 13
          'CHECK THAT IT IS AM
          intDay = Day(Now + 0.5)
          'IF IT IS PM ON A 12 HOUR CLOCK CONVERT TO 24 HOUR
          If intDay > Day(Now) Then
            intHour = intHour + 12
          End If
      End Select
      'FORMAT THE CURRENT TIME
      strStart = intHour & ":" & Minute(Now) & ":" &
      Second(Now)
      objExcel.ActiveSheet.Cells(1, 4).Value = strStart
      'CONVERT TIME INTO SECONDS
      strStart = Val(Left$(strStart, 2)) * 3600 +
      Val(Mid$(strStart, 4, 2)) * 60 + Val(Right$(strStart, 2))
      blnStart = True
      sCounter = 11
    'LEAVE 11 LINES FREE
    For sCounter = 11 To sCell
        objExcel.ActiveSheet.Cells(sCounter, 1).Value = ""
        objExcel.ActiveSheet.Cells(sCounter, 2).Value = ""
      Next
      sCell = 11
      intTime = Val(txtInterval.Text)
      cmdOK.Enabled = False
      cmdSave.Visible = False
      cmdReset.Enabled = False
      cmdCancel.Enabled = True
      cmdCancel.Visible = True
    End If
End Sub
```

```
Private Sub cmdReset_Click()
  Over_Write
  If blnOverwrite = True Then
    'RESET THE FORM
    cmdSet_Click
    tmrWLP.Enabled = False
    txtInterval.Text = "1"
    cmbParameter.ListIndex = 0
    cmdReset.Visible = False
    cmdOK.Visible = False
    cmdCancel.Visible = False
    cmdSave.Visible = False
    cmdSet.Visible = True
    cmbParameter.Visible = True
    txtInterval.Visible = True
    lblParameter.Visible = True
    lblInterval.Visible = True
    strCommand = ""
    strParam = ""
    intInterval = 0
    lblDisplay.Visible = False
  End If
End Sub
```

```
Private Sub cmdSave_Click()
  'SAVE & CLOSE THE EXCEL WORKBOOK
  With objExcel
    .ActiveWorkbook.Save
    Close_Excel
  End With
  'RESET THE FORM
  mnuFileNew.Enabled = True
  cmbParameter.Visible = False
  cmdSet.Visible = False
  cmdCancel.Visible = False
  cmdSave.Visible = False
  cmdReset.Visible = False
  cmdOK.Visible = False
  lblParameter.Visible = False
  txtInterval.Visible = False
  lblSeconds.Visible = False
  lblDisplay.Visible = False
```

```
End Sub
Private Sub cmdSet_Click()
  cmdReset.Visible = True
  cmdOK.Visible = True
  cmdOK.Caption = "Start"
  cmdCancel.Visible = True
  cmdSave.Visible = False
  cmdCancel.Enabled = False
  cmdSet.Visible = False
  cmbParameter.Visible = False
  txtInterval.Visible = False
  lblDisplay.Visible = True
  lblParameter.Visible = False
  lblInterval.Visible = False
  lblSeconds.Visible = False
  intTime = Val(txtInterval.Text)
  'SET THE QUERY INTERVAL BASED ON USER INPUT
  intInterval = Val(txtInterval.Text) * 1000
  'DETERMINE WHAT PARAMETER TO QUERY
  Select Case cmbParameter.ListIndex
    Case Is = 0
      strParam = "RM"
    Case Is = 1
      strParam = "PM"
  End Select
  sCell = 11
  'SET THE COMMAND TEXT
  strCommand = "0," & strParam & Chr$(13)
  'SET THE TIMER INTERVAL
  tmrWLP.Interval = intInterval
  'BEGIN THE TIMER
  tmrWLP.Enabled = True
End Sub
Private Sub Form_Load()
  'LOAD THE FORM IN A MAXIMSED STATE
  frmWLP.WindowState = vbMaximized
  'SET THE DEFAULT DIRECTORY
  cdlWLP.InitDir = "C:\"
End Sub
Private Sub Form_Unload(Cancel As Integer)
```

```
  If blnExcel = True Then
    objExcel.ActiveWorkbook.Save
    Close_Excel
  End If
  Unload Me
End Sub
```

```
Private Sub mnuExit_Click()
  Form_Unload (1)
End Sub
```

```
Private Sub mnuHelpAbout_Click()
  frmAbout.Show vbModal
End Sub
```

```
Private Sub MSCommWLP_OnComm()
  Dim strHour As String
  Dim strMinutes As String
  Dim strSeconds As String
  Dim strTime As String
  Dim strTotTime As String
  'RECEIVE INPUT FROM THE LODE BIKE
  strInput = MSCommWLP.Input
  If Right$(strInput, 1) = Chr$(13) Then
    strInput = Mid$(strInput, 3, Len(strInput) - 3)
    'REMOVE COMMAS FROM THE STRING
    If Left$(strInput, 1) = "," Then
      strInput = Right$(strInput, Len(strInput) - 1)
    End If
    'CALCULATE TIME IN SECONDS
    strTime = Now
    strTime = Right$(strTime, 8)
    strHour = Left$(strTime, 2)
    strMinutes = Mid$(strTime, 4, 2)
    strSeconds = Right$(strTime, 2)
    strTotTime = Val(strHour) * 3600 + Val(strMinutes) * 60 +
    Val(strSeconds)
    'DISPLAY THE CURRENT OUTPUT
    lblDisplay.Caption = strInput
    'SIZE THE LABEL
    lblDisplay.AutoSize = True
    'POSITION THE LABEL
    lblDisplay.Left = frmWLP.Width - (lblDisplay.Width +
    1000)
```

```
    Select Case blnStart
      Case False
      Case True
        'RECORD THE OUTPUT & TIME
        With objExcel.ActiveSheet
          .Cells(sCell, 2).Value = strInput
          .Cells(sCell, 3).Value = strTotTime
          .Cells(sCell, 1).Value = "= " & Val(.Cells(sCell,
          3)) & " - " & Val(.Cells(11, 3))
        End With
        'MOVE DOWN ONE ROW   .
        sCell = sCell + 1
    End Select
    strInput = ""
  End If
End Sub
```

```
Private Sub tmrWLP_Timer()
  'SEND THE COMMAND TO THE LODE BIKE
  MSCommWLP.Output = strCommand
End Sub
```

```
Private Sub txtInterval_Validate(Cancel As Boolean)
  'VALIDATE THE INPUT IN THE TIME INTERVAL BOX
  If IsNull(txtInterval) Then GoTo Error
  If Not IsNumeric(txtInterval) Then GoTo Error
  If Val(txtInterval.Text) < 1 Then GoTo Error
  Exit Sub
Error:
  MsgBox "Please input valid data", vbOKOnly, "Data
  validation"
  Cancel = True
End Sub
```

```
Public Sub New_Test()
  'LOAD THE COMBO BOX
  With cmbParameter
    .Clear
    .AddItem ("Cadence (rpm)")
    .AddItem ("Load (Watts)")
  End With
  cmbParameter.ListIndex = 0
  txtInterval.Text = "1"
  tmrWLP.Enabled = False
```

```
    cmbParameter.Visible = True
    lblInterval.Visible = True
    lblParameter.Visible = True
    lblSeconds.Visible = True
    cmdSet.Visible = True
    '9600 BAUD, EQUAL PARITY, 7 DATA, AND 2 STOP BIT
    MSCommWLP.Settings = "9600,E,7,2"
    'READ THE ENTIRE BUFFER
    MSCommWLP.InputLen = 0
    'SET ON_COMM EVENT THRESHOLD TO 1
    MSCommWLP.RThreshold = 1
    On Error GoTo Port2
    ' USE COM1
    MSCommWLP.CommPort = 1
    ' OPEN THE PORT
    MSCommWLP.PortOpen = True
    Exit Sub
Port2:
    ' USE COM2
    MSCommWLP.CommPort = 2
    ' OPEN THE PORT
    MSCommWLP.PortOpen = True
End Sub
```

```
Private Sub mnuFileNew_Click()
    'LOAD DETAILS FORM
    frmDetails.Show vbModal
    'CHECK THAT DETAILS IS SUBMITTED
    If blnDetails = False Then
      Exit Sub
    End If
    'SET THE COMMON DIALOG FLAGS
    cdlWLP.Flags = cdlOFNHideReadOnly Or
    cdlOFNExtensionDifferent _
    Or cdlOFNCreatePrompt
    cdlWLP.ShowSave
    If cdlWLP.FileName <> "*.xls" Then
      'LOAD THE EXCEL WORKBOOK
      Load_Excel
      'CHECK THAT THE FILE WAS ABLE TO LOAD
      If blnExcel = True Then
        'LOAD THE MSCOMM PARAMETERS FOR THE NEW TEST
```

```
      mnuFileNew.Enabled = False
    End If
  End If
End Sub
```

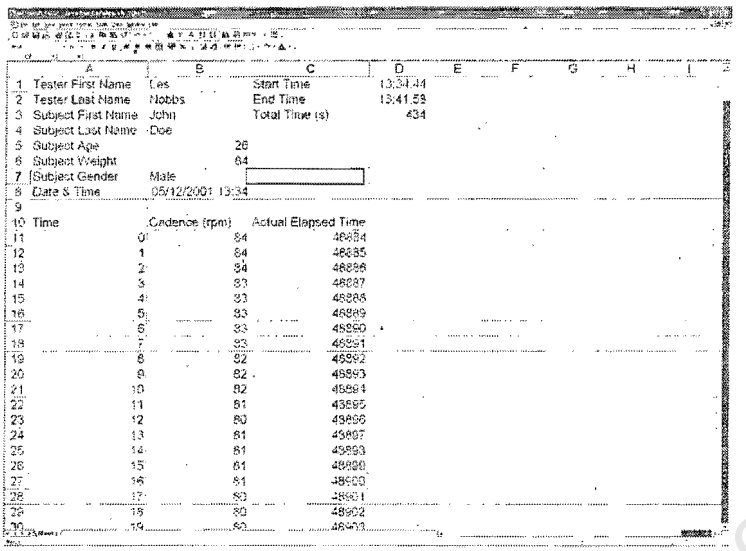
```
Public Sub Load_Excel()
  'ALERT THAT LOAD_EXCEL HAS BEEN CALLED
  blnExcel = True
  Set objExcel = New Excel.Application
  With objExcel
    'HIDE THE EXCEL SHEET
    .Visible = False
    'ADD ONLY 1 PAGE
    .SheetsInNewWorkbook = 1
    .Workbooks.Add
  End With
  'TAKE THE FILENAME FROM THE COMMON DIALOG BOX
  strFileName = cdlWLP.FileName
  'SAVE THE EXCEL FILE
  On Error GoTo InUse
  objExcel.ActiveWorkbook.SaveAs FileName:=strFileName,
  FileFormat:=xlNormal, ReadOnlyRecommended:=False,
  CreateBackup:=False
  Initial_Excel
  Exit Sub
InUse: Close_Excel
End Sub
```

```
Public Sub Initial_Excel()
  'RECORD INPUT FROM frmDETAILS IN THE EXCEL FILE
  With objExcel.ActiveSheet
    .Cells(1, 1).Value = "Tester First Name"
    .Cells(1, 2).Value = strTesterFirst
    .Cells(2, 1).Value = "Tester Last Name"
    .Cells(2, 2).Value = strTesterLast
    .Cells(3, 1).Value = "Subject First Name"
    .Cells(3, 2).Value = strClientFirst
    .Cells(4, 1).Value = "Subject Last Name"
    .Cells(4, 2).Value = strClientLast
    .Cells(5, 1).Value = "Subject Age"
    .Cells(5, 2).Value = strAge
    .Cells(6, 1).Value = "Subject Weight"
    .Cells(6, 2).Value = strWeight
```

```
    .Cells(7, 1).Value = "Subject Gender"
    .Cells(7, 2).Value = strGender
    .Cells(8, 1).Value = "Date & Time"
    .Cells(8, 2).Value = Now
    .Cells(10, 1).Value = "Time"
    .Cells(10, 2).Value = cmbParameter.Text
    .Cells(10, 3).Value = "Actual Elapsed Time"
    .Cells(1, 3).Value = "Start Time"
    .Cells(2, 3).Value = "End Time"
    .Cells(3, 3).Value = "Total Time (s)"
  End With
End Sub
```

```
Public Sub Close_Excel()
  objExcel.ActiveWorkbook.Close
  'SET THE FILENAME BACK TO DEFAULT
  cdlWLP.FileName = "*.xls"
  blnExcel = False
  Set objExcel = Nothing
  tmrWLP.Enabled = False
  If MSCommWLP.PortOpen = True Then
    MSCommWLP.PortOpen = False
  End If
End Sub
```

```
Public Sub Over_Write()
  'DETERMINE WHETHER THE USER IS AWARE THEY WILL OVERWRITE
  DATA
  Dim intChoice As Integer
  intChoice = MsgBox("Are you sure you want to overwrite
  existing data?", vbExclamation + vbYesNo, "Caution")
  If intChoice = vbYes Then
    blnOverwrite = True
  ElseIf intChoice = vbNo Then
    blnOverwrite = False
  End If
End Sub
```



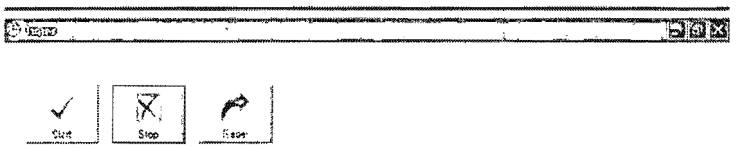
	A	B	C	D
1	Tester First Name	Les	Start Time	13:34:44
2	Tester Last Name	Nobbs	End Time	13:41:58
3	Subject First Name	John	Total Time (s)	434
4	Subject Last Name	Doe		
5	Subject Age	26		
6	Subject Weight	84		
7	Subject Gender	Male		
8	Date & Time	05/12/2001 13:34		
9				
10	Time	Cadence (rpm)	Actual Elapsed Time	
11	0	84	46884	
12	1	84	46885	
13	2	84	46886	
14	3	83	46887	
15	4	83	46888	
16	5	83	46889	
17	6	83	46890	
18	7	83	46891	
19	8	82	46892	
20	9	82	46893	
21	10	82	46894	
22	11	81	46895	
23	12	80	46896	
24	13	81	46897	
25	14	81	46898	
26	15	81	46899	
27	16	81	46900	
28	17	80	46901	
29	18	80	46902	
30	19	80	46903	

Temporal feedback

FORMS

FRMTIMER

00:00:00



00:00:21

```
Option Explicit
Dim blnValid As Boolean
Dim intTimer As Integer
```

```
Dim intInterval As Integer
Dim intDisplay As Integer
Dim intCaption As Integer
Dim strHours As String
Dim strMinutes As String
Dim strSeconds As String
Dim intSeconds As Integer
Dim intMinutes As Integer
Dim intHours As Integer
Dim intCounter As Integer
Dim intFire As Integer
```

```
Private Sub cmdReset_Click()
  intTimer = 0
  intInterval = 0
  intDisplay = 0
  txtTime.Text = ""
  txtInterval.Text = ""
  txtDisplay.Text = ""
  txtTime.Visible = True
  txtInterval.Visible = True
  txtDisplay.Visible = True
  lblTime.Visible = True
  lblInterval.Visible = True
  lblDisplay.Visible = True
  cmbTime.Visible = True
  cmbInterval.Visible = True
  cmbDisplay.Visible = True
  cmdSet.Visible = True
  cmdStart.Visible = False
  cmdStop.Visible = False
  cmdReset.Visible = False
  cmbTime.ListIndex = 0
  cmbDisplay.ListIndex = 0
  cmbInterval.ListIndex = 0
End Sub
```

```
Private Sub cmdSet_Click()
  Validate_Input
  Select Case blnValid
    Case Is = False
      Exit Sub
```

```
    txtTime.Visible = False
    txtInterval.Visible = False
    txtDisplay.Visible = False
    lblTime.Visible = False
    lblInterval.Visible = False
    lblDisplay.Visible = False
    cmbTime.Visible = False
    cmbInterval.Visible = False
    cmbDisplay.Visible = False
    cmdSet.Visible = False
    cmdStart.Visible = True
    cmdStop.Visible = True
    cmdReset.Visible = True
    cmdStart.Enabled = True
    cmdReset.Enabled = True
    cmdStop.Enabled = False
    Set_Variables
    intCounter = intInterval
    Label_Display
    intCounter = 1
End Sub
-------------------------------------------------------------------
Private Sub cmdStart_Click()
    intCaption = intInterval
    Timer1.Enabled = True
    cmdStop.Enabled = True
    cmdStart.Enabled = False
    cmdReset.Enabled = False
    intCounter = 1
End Sub
-------------------------------------------------------------------
Private Sub cmdStop_Click()
    Timer1.Enabled = False
    cmdStart.Enabled = True
    cmdReset.Enabled = True
    cmdStop.Enabled = False
    lblCounter.Caption = ""
    intHours = 0
    intMinutes = 0
    intSeconds = 0
    intFire = 0
    intCounter = intInterval
```

```
  intCounter = 1
End Sub
```

```
Private Sub Form_Load()
  Timer1.Enabled = False
  cmbTime.AddItem ("sec")
  cmbTime.AddItem ("min")
  cmbTime.ListIndex = 0
  cmbInterval.AddItem ("sec")
  cmbInterval.AddItem ("min")
  cmbInterval.ListIndex = 0
  cmbDisplay.AddItem ("sec")
  cmbDisplay.AddItem ("min")
  cmbDisplay.ListIndex = 0
  Label_Display
End Sub
```

```
Private Sub Timer1_Timer()
  If intFire >= intDisplay Then
    Timer1.Enabled = False
    Exit Sub
  End If
  Display_Time
End Sub
```

```
Public Sub Validate_Input()
  intTimer = Val(txtTime.Text)
  intInterval = Val(txtInterval.Text)
  intDisplay = Val(txtDisplay.Text)
  If intTimer > 65535 Then
    MsgBox "Interval time too long", vbOKOnly +
    vbExclamation, "Data validation"
    blnValid = False
    Exit Sub
  ElseIf intTimer < 1 Then
    MsgBox "Interval time too short", vbOKOnly +
    vbExclamation, "Data validation"
    blnValid = False
    Exit Sub
  ElseIf IsNull(txtDisplay.Text) Then
    Validity_Message
    blnValid = False
  ElseIf IsNull(txtInterval.Text) Then
    Validity_Message
```

```
  ElseIf IsNull(txtTime.Text) Then
    Validity_Message
    blnValid = False
  End If
  blnValid = True
End Sub
-------------------------------------------------------------
Private Sub txtDisplay_Validate(Cancel As Boolean)
  If Not IsNumeric(txtDisplay.Text) Then
    Validity_Message
    Cancel = True
  ElseIf txtDisplay.Text = "0" Then
    Validity_Message
    Cancel = True
  End If
End Sub
-------------------------------------------------------------
Private Sub txtInterval_Validate(Cancel As Boolean)
  If Not IsNumeric(txtInterval.Text) Then
    Validity_Message
    Cancel = True
  ElseIf txtInterval.Text = 0 Then
  Validity_Message
  Cancel = True
  ElseIf txtInterval.Text < 1 Then
    Validity_Message
    Cancel = True
  End If
End Sub
-------------------------------------------------------------
Private Sub txtTime_Validate(Cancel As Boolean)
  'VALIDATE THE ENTRY INTO THE TEXT BOX
  If Not IsNumeric(txtTime.Text) Then
    Validity_Message
    Cancel = True
  ElseIf txtTime.Text = "0" Then
  Validity_Message
  Cancel = True
  End If
End Sub
-------------------------------------------------------------
Public Sub Validity_Message()
  MsgBox "Please input valid data", vbOKOnly + vbExclamation,
  "Data validation"
```

```
Public Sub Display_Time()
  Dim strDisplay As String
  'INCREMENT SECONDS BY ONE EACH TIME THE COUNTER EVENT FIRES
  intFire = intFire + 1
  intSeconds = intSeconds + 1
  'INCREMENT MINUTES WHEN SECONDS REACH 60 AND RETURN SECONDS
  TO 0
  If intSeconds > 59 Then
    intMinutes = intMinutes + 1
    intSeconds = intSeconds - 60
  End If
  'INCREMENT HOURS WHEN MINUTES REACH 60 AND RETURN MINUTES
  TO 0
  If intMinutes > 59 Then
    intHours = intHours + 1
    intMinutes = intMinutes - 60
  End If
  'RETURN HOURS TO 0 WHEN THEY EXCEED 24
  If intHours > 24 Then
    intHours = intHours - 24
  End If
  Label_Display
End Sub
```

```
Public Sub Label_Display()
  'MAKE SURE THAT THERE ARE ALWAYS 2 DIGITS FOR HH:MM:SS
  If intHours < 10 Then
    strHours = "0" & intHours
  End If
  If intMinutes < 10 Then
    strMinutes = "0" & intMinutes
  End If
  If intSeconds < 10 Then
    strSeconds = "0" & intSeconds
  Else
    strSeconds = intSeconds
  End If
  'MAKE SURE THE CAPTION DISPLAYS IN THE CORRECT INTERVALS
  If intCounter < intInterval Then
    intCounter = intCounter + 1
    Exit Sub
  End If
```

```
  lblCounter.Caption = strDisplay
  intCounter = 1
End Sub
```

```
Public Sub Set_Variables()
  If cmbTime.ListIndex = 0 Then
  intTime = Val(txtTime.Text)
  Else
    intTime = Val(txtTime.Text) * 60
  End If
  If cmbInterval.ListIndex = 0 Then
    intInterval = Val(txtInterval.Text)
  Else
    intInterval = Val(txtInterval.Text) * 60
  End If
  If cmbDisplay.ListIndex = 0 Then
    intDisplay = Val(txtDisplay.Text)
  Else
    intDisplay = Val(txtDisplay.Text) * 60
  End If
  intTimer = (intTime / intDisplay) * 1000
  Timer1.Interval = intTimer
End Sub
```

STUDIES

I

The effect of cadence on the incidence of the VO_2max plateau

II

Evidence for anticipatory pacing strategies during supramaximal exercise lasting longer than 30 s

III

Neural regulation of pacing strategies during successive 4 km time trials

IV

Physiological effects of two levels of hyperoxia during maximal exercise in a pressure-sealed chamber

V

Reliability and interchangeability of two popular automated metabolic gas analysis systems

VI

The work of breathing does not limit the maximal exercise performance of humans at sea-level

1) THE EFFECT OF CADENCE ON THE INCIDENCE OF THE VO_2MAX PLATEAU

Introduction

For the past 80 years a plateau in oxygen consumption has been regarded as the standard by which to identify maximal aerobic capacity and cardiovascular fitness (VO_2max) (Basset et al, 2000; Howley et al, 1995; Mitchell et al, 1958; Mitchell et al, 1971; Wagner, 2000). Despite the centrality of this belief to the conduct of the exercise sciences (Noakes, 1988; Noakes, 1997), a large percentage of tested subjects fail to show any plateau in oxygen consumption during maximal exercise testing (Froelicher et al, 1974; Niemelä et al, 1980; St Clair Gibson et al, 1999; Taylor, 1941). As a result numerous substitute criteria have been proposed to identify a maximal effort (Davies, 1968; Duncan et al, 1997; Issekutz et al, 1962; Maritz et al, 1961; Niemelä et al, 1980).

The frequency with which a plateau is observed appears to be dependent on, among others, the mode of exercise (Kamon et al, 1972; McArdle et al, 1973; Miyamura et al, 1978; Moody et al, 1969), the testing protocol (Draper et al, 1999; Duncan et al, 1997; Froelicher et al, 1974; Taylor et al, 1955) and the sample population (Cunningham et al, 1977; Duncan et al, 1997; Matthys et al, 1996; Rowland et al, 1992).

Furthermore, maximum oxygen consumption is generally lower in cycling than in treadmill running in the same individuals (Åstrand et al, 1986; Kamon et al, 1972; McArdle et al, 1973). It has also been suggested that any plateau in oxygen consumption observed during maximal cycling may not identify a limiting maximal oxygen capacity. Thus Katch and Katch (1973) showed that the oxygen consumption tracked the work rate during the final stage of maximal cycling exercise, and "plateaued" in subjects who reduced their pedalling cadences and hence their work output at the end of

artefactual effect of an unrecognised reduction in work output near the end of maximal exercise.

Indeed, the parabolic relationship between oxygen consumption and pedalling frequency has been well-documented in submaximal exercise (Brisswalter et al, 2000; Buchanan et al, 1985; Hagan et al, 2000; Marsh et al, 1993; Patterson et al, 1990; Swain et al, 1992; Woolford et al, 1999). Paradoxically the nadir in oxygen consumption occurs at a lower pedalling cadence than that producing optimal mechanical efficiency (Patterson et al, 1990).

The cadence-dependent variations in VO_2 may result from changes in muscle fibre recruitment patterns (Coyle et al, 1992) in which higher pedalling cadences exceed the optimal contraction velocity of type I fibres so that a greater percentage of fast twitch type II fibres are recruited in order to maintain the power output (Citterio et al, 1984). As the duration and intensity of the exercise increases, it has been suggested that selective fatiguing of these fibres (Beelen et al, 1991) may explain a drop in the pedalling cadence (Katch et al, 1973). Even if the power output did not fall as the cadence declined, the adoption of a more oxygen-efficient cadence would cause a progressive flattening of the VO_2 curve, that is, a plateau phenomenon. Such a plateau might therefore not indicate the onset of skeletal muscle anaerobiosis, as originally interpreted by A.V. Hill and colleagues (1924).

Accordingly, the aim of this study was to examine the effect of three fixed cadence exercise protocols and one self-chosen cadence protocol on the usual measures of maximal exercise including VO_2max, peak achieved

testing in which the work rate was cadence-independent and increased as a constant ramp. We postulated that the self-chosen cadence would produce the highest measures of maximal exercise including the highest VO_2max and the highest work rate. In addition, the incidence of the plateau phenomenon would be highest in this protocol, consistent with the theory that the self-chosen cadence would be the most likely to produce a truly maximal effort including the induction of skeletal muscle anaerobiosis.

Subjects

Nine physically active subjects were recruited for the study. Ethical approval was obtained from the Research and Ethics Committee at the Faculty of Health Sciences at the University of Cape Town. Before beginning the trial, all methods associated with the trial were described to the subjects each of whom then signed an informed consent.

Protocol

Subjects performed progressive maximal ramp cycle tests at four different cadences on an electrically braked ergometer that provided a variable resistance load dependant on the pedalling cadence so that power output remained constant (Lode, Groningen, The Netherlands). Subjects pedalled at 60, 80 or 100rpm or at the individually preferred cadence (PC). Trials were separated by seven days and performed in random order. The ramp protocol consisted of a 2 min warm-up ride at 150W. Thereafter, the workload of the ramp protocol increased by 0.5W.sec^{-1} until the subject was unable to maintain the prescribed cadence to within 5 rpm during the 60, 80 and 100 rpm cadence trials, or until volitional termination in the preferred cadence trial.

Expired air analyses

For the measurement of oxygen consumption (VO_2), carbon dioxide production (VCO_2) and minute ventilation (V_E), subjects wore a mask covering the nose and mouth and inhaled air across a single low resistance valve. The expired air passed over a hot wire anemometer to determine ventilatory volume and a sample was drawn through an on-line breath-by-

breath gas analyser (Vmax 229 Series, Sensor Medics, California). Before each test the pneumotachograph was calibrated with a Hans Rudolph 5530, 3L syringe and the gas analyser by span gases composed of 25.8% O_2: 0% CO_2 and 15.6% O_2: 4.1% CO_2. Oxygen consumption and CO_2 production were calculated using conventional Haldane equations and averaged over 30 seconds. Maximum oxygen consumption (VO_2 max) was defined as the highest VO_2 measured during the test.

Heart rate and cadence

Heart rate (HR) was recorded every 10 seconds using a Polar Accurex Plus heart rate monitor (Polar Electro.Kempele, Finland). The data were downloaded via an interface into hrm files after completion of the trial. Maximum HR was taken as the highest HR recorded at any stage during the test. Cadence was recorded every second via a software program designed in this laboratory. The cadence was displayed prominently on a screen in front of the subjects and the researchers gave verbal encouragement when the cadence dropped below the prescribed rate.

Statistics

Data for submaximum VO_2, VCO_2, V_E and power output were averaged over 30 s from 0 to 330 s for all subjects to avoid the confounding effect of subject dropout, which began after 330 seconds of the test. For the comparison of VO_2, VCO_2 and V_E approaching fatigue, data were averaged retrospectively over 30 s from the point of fatigue. For maximum and submaximum data, a repeated measures Analysis of Variance was used to assess differences between and within the trials. Once main effects were identified, individual differences between the means were located using

All data are expressed as mean ± standard deviation (S.D.).

Maximal values of VO_2, VCO_2, V_E and power output

The VO_2max was not different between conditions (60 rpm = 4.9 ± 0.4 L.min^{-1}; 80 rpm = 4.7 ± 0.7 L.min^{-1}; 100 rpm = 4.9 ± 0.6 L.min^{-1}; PC = 4.8 ± 0.5 L.min^{-1}) (Figure 1). Neither peak rates of CO_2 production (60 rpm = 5.7 ± 0.6 L.min^{-1}; 80 rpm = 5.5 ± 0.7 L.min^{-1}; 100 rpm = 5.7 ± 0.7 L.min^{-1}; PC = 5.7 ± 0.7 L.min^{-1}), maximal minute ventilation (60 rpm = 129 ± 12 L.min^{-1}; 80 rpm = 128 ± 20 L.min^{-1}; 100 rpm = 139 ± 16 L.min^{-1}; PC = 140 ± 22 L.min^{-1}) nor peak power output (60 rpm = 378 ± 24 W; 80 rpm = 376 ± 32 W 100 rpm = 372 ± 39 W; PC = 383 ± 33 W) were influenced by the pedalling cadence (Figure 1). Maximal heart rates were also not influenced by cadence (60 rpm = 175 ± 5 beats.min^{-1}; 80 rpm = 182 ± 8 beats.min^{-1}; 100 rpm = 183 ± 10 beats.min^{-1}; PC = 184 ± 10 beats.min^{-1}) (Figure1).

Submaximum values of VO_2, VCO_2, V_E and RER

Figure 2 shows changes in VO_2, VCO_2, V_E and RER for the first 6 minutes of the exercise test in all 9 subjects. Thereafter there was progressive subject fallout so that continuous, complete data for all these measurements are not available. Submaximum VO_2, VCO_2, V_E and RER were not different in any of the conditions. Figure 3 shows these same variables but in the final 360 s preceding the point of exercise termination in all 9 subjects. These data show that VO_2 and V_E in the final 360 s of the trial were also not influenced by the pedalling cadence.

In accordance with the methods employed by Taylor et al (1955), we determined that the mean increase in VO_2 across two consecutive 30 s periods from 240 s to 90 s preceding fatigue (0 s) was 178 $mL.min^{-1}$ (Figure 3), which is similar to the values found in other studies (Barstow et al, 1996; Walsh et al, 1995). Therefore an increase of less that 90 $mL.min^{-1}$ across two consecutive 30 s time periods was used as the criteria for defining a plateau in oxygen consumption (Figure 5). However to avoid the error of describing a plateau where none existed (Glassford et al, 1965), subjects were required to exhibit two consecutive increments in VO_2 of less than 90 $mL.min^{-1}$. Based upon these parameters, the "plateau phenomenon" was exhibited by one subject in the 60 rpm trial, three subjects in the 80 rpm trial, one different subject in the 100 rpm trial and none in the preferred cadence trial. Thus of 36 trials only 5 (17%) displayed a plateau phenomenon and no individual consistently displayed a plateau in all trials. Indeed, only one subject showed the plateau phenomenon on more than one occasion and then only twice. In no case in which a plateau was identified, was the VO_2max for that trial the highest attained by the subject in the entire study. Thus VO_2max values during the "plateau test" in these subjects was 4.4 ± 0.4 $L.min^{-1}$, whereas the VO_2max during a "non-plateau" test was 4.5 ± 0.4 $L.min^{-1}$.

Cadence

The mean cadence maintained in the fixed cadence trials was significantly different as required by the experimental protocol (Figure 4). The preferred cadence trial produced cadences (83.5 ± 6.4 rpm) that were significantly different from the 60 (61.8 ± 0.6 rpm; $p < 0.05$) and 100

preferred cadence trial declined significantly towards the end of the trial (Figure 4) ($p < 0.05$) whereas by design, cadence did not fall near the end of exercise in the three fixed cadence trials.

There were two important findings and one unexpected discovery in this study. The first important finding was that none of the measures of maximal exercise including VO_2max, maximum work rate and maximum heart rate were different between trials. Thus whether the cadence was pre-set or self-selected, the measured data during maximum exercise were unaffected.

Previous researchers have found that VO_2max and exercise performance are compromised at higher cadences (Buchanan et al, 1985; McNaughton et al, 1996). However the cadences employed in those studies (120 and 110 rpm, respectively) were higher than the highest cadence of 100 rpm used in this study. In addition none of those studies used a ramp protocol as in this study. This study therefore suggests that a true VO_2max can be achieved with the use of a ramp protocol, regardless of whether the cadence is fixed between 60 – 100 rpm or whether it is self-chosen.

The second important finding of this study was the very low incidence (14%) of a true plateau in oxygen consumption during all the trials and its complete absence in the self-chosen cadence trial. This is the lowest incidence of the "plateau phenomenon" yet reported in the literature using the traditional criteria. The probable explanation for this extremely low incidence was the ramp protocol that was used. Weston and Gabbett (Weston et al, 2001) recently showed that ventilatory parameters are highly reproducible in a 30 $W.min^{-1}$ ramp protocol and early on Taylor (1941) recognised that the ideal testing protocol for a maximum effort would be a continuously increasing workload. However, "this was not feasible with the available apparatus" (Taylor, 1941). Likewise, the early testing

was described were limited by gas collection and measurement techniques (Froelicher et al, 1974). However, the widespread adoption of electrically braked cycle ergometers and online breath-by-breath gas analysers for exercise testing (Hughson et al, 1982; Myers et al, 1990; Myers et al, 1992; Niemelä et al, 1980; Zhang et al, 1991) has seen a progressive reduction in the incidence of the plateau phenomenon so that more modern studies report this incidence at between 8 and 30% (Draper et al, 1999; Froelicher et al, 1974; Niemelä et al, 1980; Rowland et al, 1992). Furthermore there is strong evidence that the VO_2 plateau is a transient phenomenon that is also present during submaximal exercise (Myers et al, 1989; Myers et al, 1990) and the large variability in the change in VO_2 that accompanies consistent changes in work rate has caused some authors to describe the determination of a plateau as "meaningless" (Myers et al, 1990). Moreover others report that VO_2 might still be increasing at exhaustion during maximal exercise (Glassford et al, 1965). We have also recently shown that the plateau phenomenon occurs infrequently in Olympic athletes (Doherty et al, 2002), the group in which the phenomenon should be the most likely to occur if superior motivation is required to induce the supposed skeletal muscle anaerobiosis that purportedly produces skeletal muscle anaerobiosis. Thus this study confirms that the plateau phenomenon is not a valid measure of maximum effort (Duncan et al, 1997) since it occurs uncommonly in studies in which a ramp protocol is used, regardless of the cadence that is tested.

The novel and perhaps most important finding of this study was that the cadence during the self-chosen cadence trial declined significantly during the last two minutes of the trial (Figure 4) even though the VO_2 continue to rise (Figure 3).

exercise physiology (Noakes, 2000), this progressive reduction in cadence near the point of fatigue would be explained by the accumulation in the exercising leg muscles of fatigue-inducing metabolites once the metabolic demands of the exercising muscle exceeded the ability of the cardiovascular system to deliver sufficient oxygen, thereby inducing skeletal muscle anaerobiosis.

However it is difficult to conceive how the build-up of such postulated metabolites could disrupt the skeletal muscle contractile processes and selectively reduce the cadence in one trial but not at the same work rate in the other trials since the production of such "peripheral fatigue" must be dependent on the attainment of a threshold work rate and VO_2. Rather the progressive reduction in cadence during the final two minutes of the self-chosen cadence trial must reflect an altered pattern of central neural recruitment that was overridden by conscious control in those trials in which the cadence was preset. This anticipatory manner in which cadence declined in the preferred trial provides indirect evidence for an altered central neural regulation of maximal exercise performance (Davies et al, 1986; Gandevia et al, 1996), which is further supported by findings of muscle reserve at fatigue (Kawakami et al, 2000; Loscher et al, 1996; McKenzie et al, 1992; Newham et al, 1991; St Clair Gibson et al, 2001; Taylor et al, 2000a; Taylor et al, 2000b).

In summary, this study shows that the ramp protocol produces a low percentage of the "plateau phenomenon" and that the choice of cadence either preset or self-selected at rates between 60 and 100 rpm does not influence any of the measured physiological variables. These findings are not consistent with the theory that maximal exercise terminates only after

the onset of skeletal muscle anaerobiosis identified by the "plateau phenomenon", according to the traditional A.V. Hill Cardiovascular/Anaerobic model of exercise (Noakes, 2000).

Furthermore, the finding that the maximum values for the physiological variables measured at exhaustion were independent of the preset or indeed the self-selected cadence, argues against the value of specific cadence-dependent recruitment of specific muscle fibre groups for peak performance. Rather the finding that these maxima were cadence-independent suggests either that the same muscle fibre proportions are active at exhaustion, or that maximum exercise can be supported by varieties of different proportions of muscle fibres. Finally, the reduction in cadence at the self-selected cadence near the end of exercise indicates that neural regulation of the movement pattern altered the pedalling frequency in anticipation of the termination of exercise. In cycling tests in which work rate is cadence dependent, this would produce an artefactual "plateau phenomenon" as originally recognised and reported by Katch and Katch (1973) nearly three decades ago.

Figure 1 Mean maximum values of VO_2, power output, minute ventilation and heart rate during maximal exercise performed at 60, 80, 100 rpm and a self-selected cadence.

Figure 2 Submaximal VO_2, VCO_2, V_E and RER for the initial 360 s of progressive maximal exercise performed according to a ramp protocol at 60 (●), 80 (□), 100 (×) rpm and a self-selected (◇) cadence.

Figure 3 VO_2, VCO_2, V_E and RER for the final 330 s of progressive maximal exercise performed according to a ramp protocol at 60 (●), 80 (□), 100 (×) rpm and a self-selected (◇) cadence.

Figure 4 Comparison of cadence for the final 330 s of progressive maximal exercise performed according to a ramp protocol at 60 (●), 80 (□), 100 (×) rpm and a self-selected (◇) cadence.

* Significantly different from –60 s to fatigue (self-selected cadence trial) ($p < 0.05$)

γ Significantly different from –30 s to fatigue (self-selected cadence trial) ($p < 0.05$)

δ Significantly different from fatigue (self-selected cadence trial) ($p < 0.05$)

Figure 5 The change in oxygen consumption across successive 30 s periods for the final 330 s of progressive maximal exercise performed according to a ramp protocol at 60 (●), 80 (□), 100 (×) rpm and a self-selected (◇) cadence

FIGURE 1

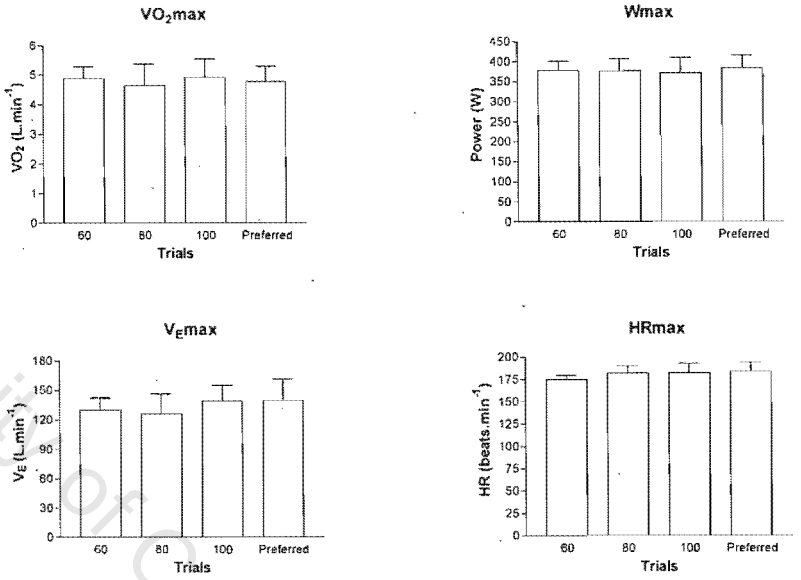


FIGURE 2

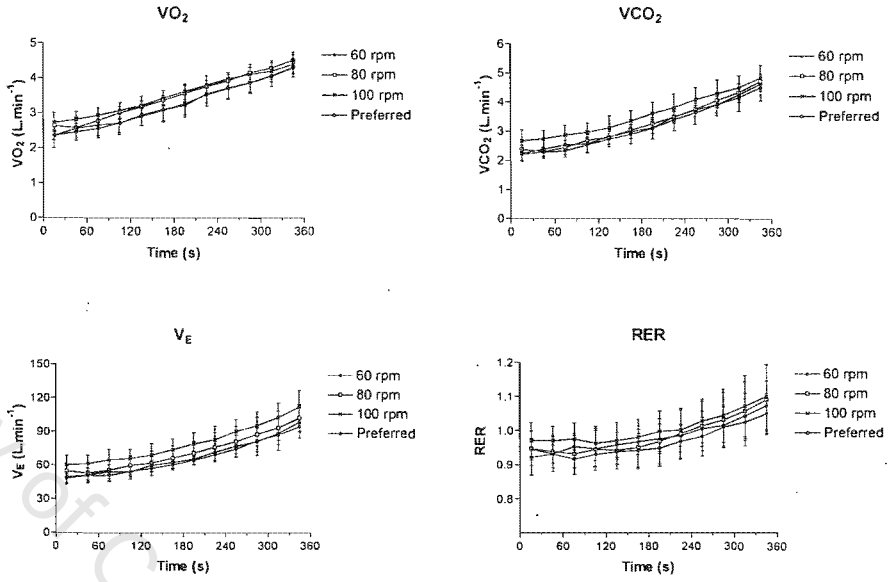


FIGURE 3

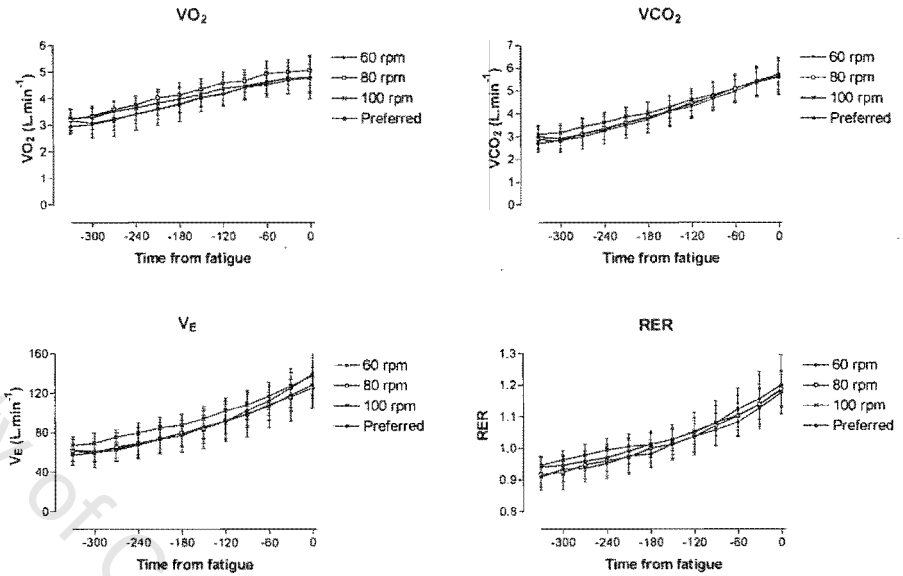


FIGURE 4

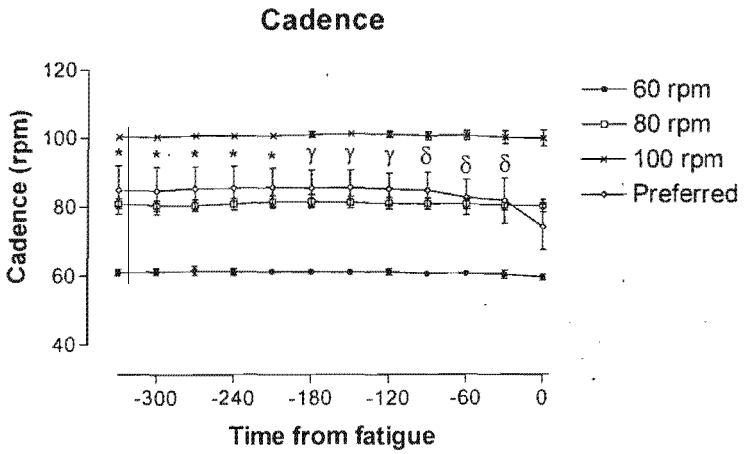
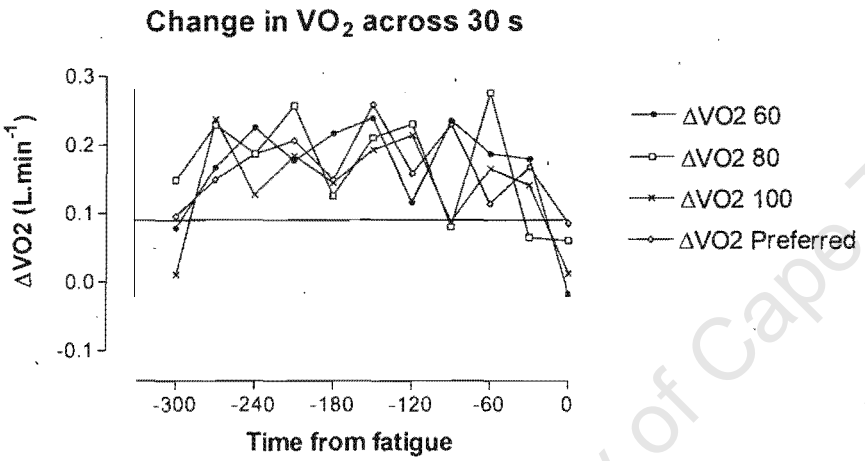


FIGURE 5



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ii) EVIDENCE FOR ANTICIPATORY PACING STRATEGIES DURING SUPRA-MAXIMAL EXERCISE LASTING LONGER THAN 30 S

Introduction

For the last 30 years researchers have used the Wingate Anaerobic Test (WAnT), or a variant thereof, as a means of quantifying anaerobic performance in absolute terms of power output which is then related to the maximum capacities of specific metabolic pathways. Traditionally the WAnT uses a 30-second cycle test protocol, performed against a constant force, in which subjects are instructed to cycle as hard as they can for the duration of the test. The three indices commonly derived from the WAnT are: i) peak power index (PPI), the highest power output obtained during the trial: ii) mean power index (MPI), the average power sustained over the duration of the trial; and iii) fatigue index (FI), the drop-off in power between the PPI and the final power output reading.

It was thought that during the initial 5 – 10 seconds of exercise energy is derived solely from alactic, phosphogenic pathways after which the metabolic fuel for the rest of the exercise bout is obtained from anaerobic glycolysis. Subsequent research has shown that, contrary to this belief, lactate accumulation begins within the first 10 seconds of supramaximal exercise (Jacobs et al, 1983; Bogdanis et al, 1996) and that mitochondrial oxidative ATP synthesis increases almost immediately at the onset of exercise (Nioka et al, 1998).

Despite this aerobic component of undetermined magnitude, the WAnT is considered to be largely dependant on anaerobic metabolism (Serresse et al, 1988) and the associated fatigue has been mainly attributed to the fall in pH (Cherry et al, 1997) that changes potassium concentration (Brody et al, 1991) and/or interferes with calcium release (Allen et al, 1992), impeding the ability of the muscle to contract (Mortimer et al, 1970; di Prampero et al, 1981;

twitch fibres (Beelen and Sargeant, 1991; Hautier et al, 1998).

The WAnT may not have been designed to study muscle contractility or fatigue (Bar-Or, 1987) but it has been suggested (Green et al, 1995) that observing the effects of such all out efforts could provide insight into physiological and neuromuscular capabilities. While this peripherally mediated fatigue might account for some of the drop-off in power output observed during the WAnT, electromygraphic (EMG) signal recordings have revealed a decline in iEMG activity towards the end of the test, which suggests the occurrence of central fatigue (Vandewalle et al, 1991; Hunter et al, 2003). Indeed, the fact that the fall in power in the Wingate test is explained by the falling cadence (Katch and Katch, 1973) can really only be explained by central, neural regulation since it is not clear how peripheral fatigue alone can produce the necessary changes in motor recruitment necessary to cause the progressive and marked reduction in cadence. Although the 30 second duration of the WAnT is generally considered optimal (Margaria et al, 1969; Green, 1995), a number of authors have suggested that it may not be sufficiently long to measure the total anaerobic capacity (Vandewalle et al, 1987; Bacharach and von Duvillard, 1995; Calbet et al, 1997). The difficulty in extending the protocol beyond 30 seconds is the adoption of pacing strategies by subjects to ensure that they are able to complete the test (Bar-Or, 1987; Bacharach and von Duvillard, 1995). To prevent the adoption of such a conscious pacing strategy, it has been suggested that subjects should not be made aware of the elapsed time (Katch and Weltman, 1979). More recently the concept that subjects subconsciously pace themselves during exercise on the basis of prior experience has been developed (Ulmer, 1996; St Clair Gibson et al, 2001).

adopted during events lasting 1 - 6 minutes (Hagerman, 1984; Foster et al, 1993; Foster et al, 1994) and the optimal pacing strategies over these periods (Ingen Schenau et al, 1994). However, to the authors' knowledge, no study has yet evaluated the possible presence of pacing during bouts of supra-maximal exercise. The existence of a pacing strategy would suggest that substrate depletion or metabolic accumulation might not be the immediate cause of the power output profile during a WAnT.

Accordingly the aim of this study was to determine whether deception and temporal manipulation could identify whether a subconscious pacing strategy exists during a standard and modified WAnT lasting between about 30 and 36 seconds.

Methods

Eight healthy males volunteered for this study. The age and body mass (mean ± SD) were 22 ± 2.5 years and 76.5 ± 6.9 kg, respectively. All subjects were physically active and each signed an informed consent before the study. The study was approved by the Research and Ethics Committee of the University of Cape Town, Faculty of Health Sciences.

Subjects performed six Wingate Anaerobic Tests on a Monarck friction-braked cycle ergometer (814E). Trials were held one week apart at the same time of day (Hill and Smith, 1991; Reilly and Down, 1992) and the order of the trials was randomised. One week prior to the start of the trial subjects performed a habituation Wingate test.

Standardisation procedure

A load of 0.09 $kg.kg^{-1}$ body mass (Dotan and Bar-Or, 1983; Patton et al, 1985) was administered by placing calibrated weights on a weight pan, which exerted a resistive force against the flywheel, at the onset of exercise. Workloads were set to the nearest 0.1 kg. Saddle height was recorded on the first visit to the laboratory and the same height was used in all subsequent trials (Burke, 1986). Subjects were strapped to the saddle to avoid standing on the pedals (Vandewalle et al, 1987). Pedal crank length was constant (Inbar et al, 1983) and all subjects used cleated cycling shoes (LaVoie et al, 1984). The warm up was standardised to 2 minutes unloaded pedalling (Inbar and Bar-Or, 1975; Hawley et al, 1989). Before the start of each trial subjects were instructed to pedal as fast as possible and to attempt to maintain that cadence velocity for the duration of the test. All tests were conducted from a standing start (Kaczkowski et al, 1982). The same investigators offered encouragement throughout the trial to minimise motivational differences (Bar-Or, 1987).

Time feedback during the trial was provided on an LCD screen that displayed elapsed time.

Subjects were informed that they were completing four 30 second, one 33 second and one 36 second trial. However, they actually completed two trials of 30 (30_1 and 30_2), 33 (33_D and 33_I) and 36 (36_D and 36_I) seconds each. The suffixes D and I denote the deception trial and informed trial, respectively. A computer application altered the rate at which the LCD counter displayed second intervals. Therefore during the two deception trials the display time showed a 30 second count for the 33 and 36 second duration of the respective tests.

Data capture

The angular velocity of the flywheel was calculated every 36° from sensors attached to the flywheel. Pedal revolutions per minute were then derived from the formula:

$$\text{Rpm} = \frac{\text{Pedal revolutions}}{\text{Flywheel angular displacement}} \times \frac{\text{Flywheel angular displacement}}{\text{time}}$$

Data capture occurred every 0.5 seconds and the power generated on the Monarch bicycle was calculated using the following formula:

$$\text{Power} = \text{Load mass} \times \text{rpm}$$

Indices

The PPI was calculated as the highest average power over any 3 second period (Bar-Or, 1987), MPI as the average power over the entire trial and FI as the fractional decrease in power during the test (McCartney et al, 1983):

$$\text{FI} \quad \frac{\text{PPI} - \text{FP}}{\text{PPI}}$$

where FP is the power averaged over the final 3 seconds of the test.

Statistical analysis

Power output data for all calculations were averaged over 3 seconds. Calculations for MPI and FI during the modified trials were determined over the entire duration and over the first 30 s. An analysis of variance was used to assess differences between and within the trials. Once main effects were identified individual differences between the means were located using Tukey's HSD *post hoc* procedure. Significance was accepted at $P < 0.05$. All data were expressed as mean ± standard deviation (S.D.).

Results

On completion of the study the subjects were unable to identify on which occasions they performed the deception trials.

Power output

Power output was uncorrected for inertia. There were no differences in power output up to 30 s between any of the trials (Figure 1). However in the 36 s trials, the power output was significantly lower at 36 s in the deception trial compared with the informed trial (392 ± 32 W vs. 470 ± 88 W; $p < 0.001$).

Peak power index

There were no significant differences in the magnitude of PPI between any of the trials (30_1: 1055 ± 84 W; 30_2: 1076 ± 97 W; 33_D: 1061 ± 98 W; 33_I: 1047 ± 107 W; 36_D: 1056 ± 83 W; 36_I: 1055 ± 74 W) (Figure 2a) nor did the time at which peak power occurred differ (30_1: 5.8 ± 1.0 s; 30_2: 5.3 ± 1.5 s; 33_D: 5.4 ± 1.1 s; 33_I: 4.9 ± 2.6 s; 36_D: 4.6 ± 1.0 s; 36_I: 4.7 ± 1.0 s) (Figure 1).

Mean power index

The MPI for the 36 s trials (36_D: 714 ± 76 W; 36_I: 713 ± 78 W) were significantly lower than for either of the control 30 s trials (30_1: 745 ± 65 W; 30_2: 764 ± 82 W) ($p < 0.05$), but not different from the 33 s trials (33_D: 748 ± 87 W; 33_I: 734 ± 100 W) (Figure 2b). The MPI for the 36 s trials also decline significantly from their value at 30 s (36_D: 764 ± 83 W; 36_I: 755 ± 79 W) where after there were no differences between any trials.

Fatigue index

The FI for the 36 s deception trial (63 ± 4.2%) was significantly greater than all other trials (30_1: 50 ± 7%; 30_2: 49 ± 3%; 33_I: 51 ± 3%) ($p < 0.05$) except the 36 s informed trial (56 ± 7%) and the 33 s deception trial (54 ± 3%) (Figure 1c). There was no difference in the FI at 30 s between any of the trials. The FI in the 36 s deception trial declined significantly from 30 s to 36 s (50 ± 10% vs. 63 ± 4%) ($p < 0.001$).

Discussion

The first important finding of the study was that the power output during the first 30 seconds of all trials was similar, regardless of the final duration of the trial. This finding is surprising, if it is believed that muscle energy depletion alone acting peripherally, limits such exercise. Rather it would be predicted that the same amount of chemical energy would allow a faster rate of energy expenditure during the shorter exercise durations. Instead, this finding suggests that power output during the Wingate test is controlled by factors other than purely the magnitude of the skeletal muscle energy reserves and the maximum rate at which such reserves can be depleted.

Indeed the second novel finding of this study was that power output dropped significantly more over the last 3 s of the 36 s deception trial compared with the informed trial. This occurred even though subjects were not able to consciously differentiate between the duration of the longer deception trials and the standard 30 s Wingate trial.

The finding that subjects were able to perform more work when performing exercise, the duration of which they had been reliably informed about than when misinformed, indicates that central neural factors other than peripheral metabolite accumulation, determines the power output profile of the Wingate test.

Indeed, the fall-off in power during the Wingate test has been attributed to the early selective fatiguing of fast twitch skeletal muscle fibres (Beelen and Sargeant, 1991) once the optimum velocity for maximal contractions of slower muscle fibres has been exceeded. But, it has also been shown that the decline in iEMG activity, accounts for nearly 30 percent of the drop-off in power at the end of supra-maximal exercise (Hunter et al, 2003;Vandewalle et al, 1991). Furthermore, the power output profile of the Wingate test reflects solely the

change in the cadence (Katch and Katch, 1973), which must be centrally regulated in the brain. Changes in power output generated by the brain could, however, be in response to peripheral metabolic changes in the active muscles.

Indeed, the presence of a central neural component to pacing and fatigue has long been recognised as a factor influencing power output during supra-maximal exercise. Pilot studies at the Wingate Institute during the development of the Wingate Anaerobic Test showed a propensity for subjects to start at slower cadences in trials that lasted longer than 30 s (Bar-Or, 1987). This tendency was also observed by Katch and Weltman (1979) who remarked that the duration of the trial should not be revealed to the subjects lest they "pace themselves and not produce an initial all-out effort". In a study on elite Alpine skiers (Bacharach and von Duvillard, 1995), trial subjects were instructed to ease up after they had achieved peak power so that they would be able to maintain more constant effort for the remainder of the 90 s trial, implying that some form of pacing is necessary to complete extended supra-maximal tests.

An even pace has long been regarded as the most efficient strategy to employ during any exercise and this belief appears to be supported by evidence that during an even-paced Wingate trial, blood lactate concentrations are lower, blood pH is higher and recovery is faster, compared with an all-out trial, in which the same total amount of work is performed (Cherry et al, 1997). In contrast Ingen-Schenau et al (1994) argue that in events lasting less than 80 s, the optimal pacing strategy is all out effort, even if this strategy produces a rapid drop-off in power at the end of the race. They suggested that an even-paced strategy should only be used in exercise of a longer duration. Our data do not address this question.

It has been speculated that muscle pH provides the sensory feedback limiting central command of motor unit recruitment and intramuscular metabolism (Kent-Braun, 1999) so that athletes adjust their pace in order to ensure that a critically low pH is not reached even at the end of a maximum effort (Foster et al, 1994). This is supported by evidence of a continuous fall in intramuscular pH from 6.94 to 6.82 between 10 and 20 s in all-out exercise (Bogdanis et al, 1998), mirroring the decline in power output. The fall in power output ensures that the extent of the fall in pH is regulated.

Ulmer (1996) extended this concept by proposing the existence of a programmer during exercise that regulates work based upon the remaining duration of an activity. In other words the effort required in performing an activity is anticipated prior to the commencement of the activity and the intensity of exertion is regulated according to calculations based on previous experience. This governor acts as a protective regulator of power output to prevent the development of a metabolic crisis that would damage the integrity of the muscle fibres (Sargeant, 1994).

Although there were significant differences in power output at 36 s when the subjects were deceived as compared to the informed trial, no differences were present at the end of the 33 s trials indicating that the modification in afferent control, causing a reduction in power in the last 3 seconds, must occur after 33 s but before 36 s. This is in agreement with the speculation of Hunter et al (2003) that 30 s was too short a duration for a change in recruitment strategies based upon feedback from intramuscular metabolism but predicted that the influence of this feedback loop on central motor control would have to come into effect if the exercise was sufficiently prolonged.

Evidence that the extent of muscle recruitment is controlled centrally during prolonged exercise has been presented by St Clair Gibson et al (2001) in a

in the neural drive despite less than 20% of the muscle mass being recruited. They concluded that the early decline in neuromuscular activity during prolonged exercise explained the reduced power output experienced by their subjects.

During the informed trial the subjects prepared themselves for an effort that would last 36 s. During the 36 s deception trial, though, the subjects were only primed for a 30 s effort and despite confirmatory but deceptive evidence in the form of a clock, that was 6 seconds slow, there was still a disparity between their actual and possible power outputs (Figure 1). As the subjects were not consciously aware of the deception, this finding indicates that the deception was detected at a subconscious level but not a conscious level since the reduction in power output over the extra time was not consciously perceived. If the duration of the 36 s trials had been extended beyond 40 s the subjects may have employed a more obvious coping strategy. However, it is unlikely that subjects would have been deceived, that is they would not have realised that a deception was in place, by such a large (33%) discrepancy between the real and simulated time. Accordingly, this type of experiment may not be possible.

Rather we conclude that the subjects did detect the time discrepancies but ignored or filtered the conscious knowledge as incorrect based upon what they had been told and the visual cues from the slow-running clock. However, the findings of the present study suggest that the "lag" phase between afferent input and subconscious awareness of discrepancies between expected and actual time must be between 3 and 6 s during an exercise lasting up to 36 s, that is, approximately 12% of the total duration of the activity. More research is needed to determine the degree to which subjects can accurately assess temporal deceptions during exercise.

the subjects started out at a set work rate, although whether this is paced and submaximal itself cannot be determined from this study. The similar fatigue profiles over the initial 30 s for all the trials suggest that there was no difference in the pacing strategy employed for the different duration trials. However, the sudden decline in power output of the last 3 s of the 36 s deception trial may provide evidence for a pre-programmed "end point" that is different from the ultimate fatigue point. Once the anticipated end point is reached, the power output declines rapidly. It has been demonstrated that even in maximal sprint intervals, subjects maintain a reserve allowing an increase in power output over the last sprint consequent to an increased neural drive (Kay et al, 2001).

In summary, this study indicates the presence of a pre-programmed "end point" based on the anticipated exercise duration as a result of previous experience in a Wingate test. Furthermore the similarity in pacing strategy in all informed trials regardless of duration suggests that the pacing strategy is centrally regulated and is independent of the total work to be performed, at least for up to 36 seconds of supramaximal exercise.

Figure 1 Comparison of power output profile for the two 30, 33 and 36 s Wingate Anaerobic Tests

Figure 2 Peak power, mean power and fatigue indices at 30 s and at the completion of the Wingate Anaerobic Tests

* significantly different from the 36s deception and 36 s informed trial ($p < 0.05$)

λ significantly different from the 36s deception ($p < 0.05$)

FIGURE 1

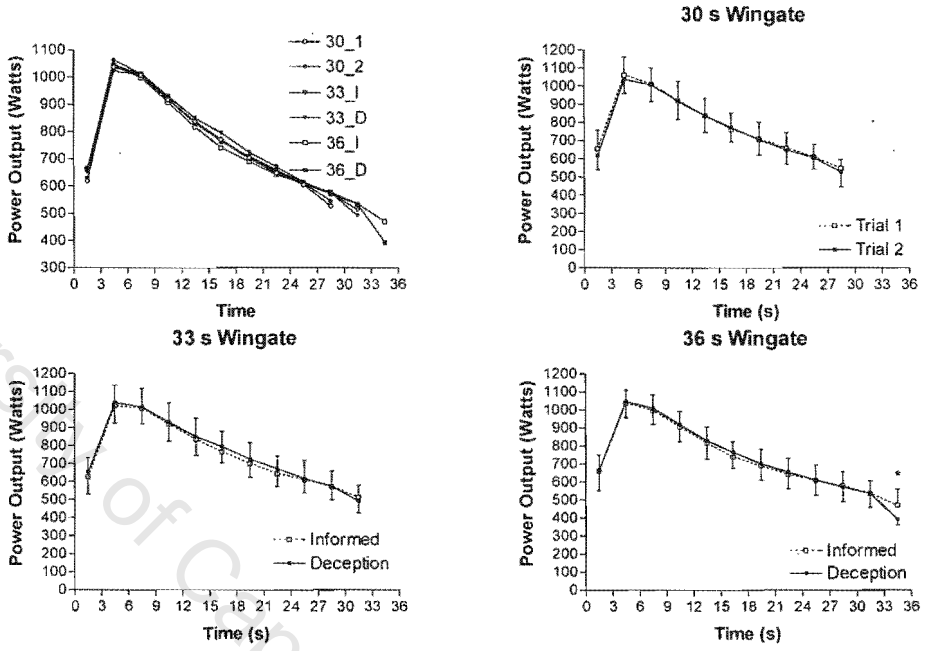
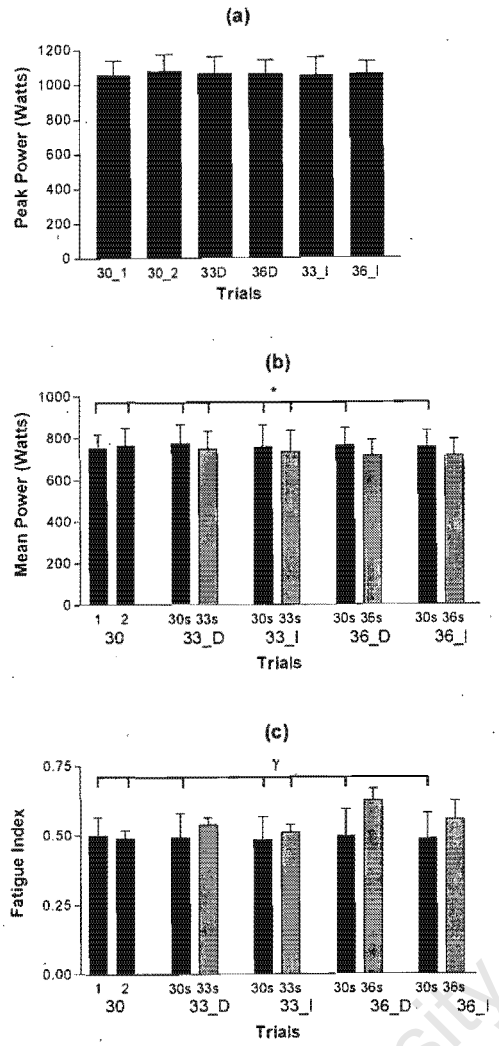


FIGURE 2



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III) NEUROMUSCULAR REGULATION OF PACING STRATEGIES DURING SUCCESSIVE 4 KM TIME TRIALS

The capacity to produce and maintain power output decreases rapidly during bouts of high intensity exercise (Bar-Or, 1987; Withers et al, 1991). Therefore, in order to sustain a high power output in events lasting longer than several seconds, athletes must adopt a pacing strategy to delay fatigue and optimise performance. The typical pacing strategy comprises several stages: a short initial period of high power output followed by a sharp reduction to a power output, which is usually maintained until the final period of the exercise bout when power output may again increase (Hagerman, 1984).

It is usually believed that these changes in power output are determined by the development of a critically low muscle pH that impairs skeletal muscle contractile function (Metzger et al, 1987; Nakamaru et al, 1972), so-called 'peripheral fatigue'. However, this peripheral model of fatigue does not satisfactorily explain all the known features of exercise fatigue (Kay et al, 2001; Noakes, 1997; Noakes, 2000; Ulmer, 1996) most notably the phenomenon of the "lactate paradox" of high altitude. This paradox occurs during peak exercise at extreme altitude and in which exercise terminates at low blood lactate concentrations, often no higher than resting concentrations (Hochachka et al, 2002; Sutton et al, 1992).

Foster *et al* (1994) have proposed the alternate theory in which the pacing strategy is under central neural control. Indeed this theory that the central nervous system regulates athletic performance was first proposed over a century ago (Waller, 1896). But, the complexity of quantifying any central neural regulation of exercise performance has influenced researchers to focus on the peripheral, skeletal muscular determinants of fatigue and exercise performance with, until recently, less attention on any central component, (Andersen, 1968; Gandevia, 2001; Noakes, 1988).

with short periods of recovery between exercise bouts, represents one of the most intense forms of physical activity. Since the activity is repetitive, athletes must adopt a pacing strategy within the first interval to ensure that they can produce repetitive intervals with similar total work output. In order to determine any contribution of the central nervous system to the regulation of this pacing strategy, we measured the work output and associated changes in physiological, integrated electromyographic (iEMG) and metabolic parameters in consecutive 4 km cycling intervals performed by highly trained cyclists in the laboratory. We theorised that central regulation would produce pacing strategies that were more similar across intervals and in which iEMG activity would follow the changes in power output. In contrast, peripheral regulation would produce pacing strategies that were less similar across intervals; in which changes in power output would mirror changes in blood lactate concentrations, and in which power output would steadily decline towards the latter stages of the exercise bout despite a progressive increase in iEMG activity. In addition, a high proportion of all available motor units would be recruited during each interval.

Methods

Subjects

Seven highly trained, competitive male cyclists were selected to participate in this study. These subjects were chosen because they were well trained, accustomed to high intensity exercise and familiar with laboratory testing since they frequently participated in previous trials in this laboratory. At the time of investigation, they were cycling 400-800 km.wk^{-1}. The study was conducted with the approval of the Ethics in Human Research Committee of the Faculty of Health Sciences at the University of Cape Town; prior to the trial all subjects were informed of the nature of the investigation, after which they gave written informed consent. Subject characteristics are described in Table 1.

Kingcycle ergometry system

Each subject completed two trials in the laboratory. On the first occasion maximal power output and maximal oxygen consumption (VO_2max) was measured. On the second occasion seven days later, subjects performed three consecutive, 4-km time-trials (TT) with a 17-minute rest between each. All tests were conducted on a Kingcycle ergometry system (Kingcycle Ltd, High Wycombe, U.K.) that allowed each cyclist to ride his own bicycle in the laboratory. Previous studies have shown that performance tests conducted on these ergometers have good reliability when compared to standard laboratory ergometers (Lindsay et al, 1996; Palmer et al, 1996; Schabort et al, 1998).

VO2max test

On their first visit to the laboratory, cyclists completed the maximal incremental exercise test (MIE) to exhaustion during which oxygen consumption (VO_2), power output and heart rate (HR) were recorded for the

duration of the test. After a 10-15 min warm-up at a self-selected intensity, the test commenced at a workload of 200 W. Thereafter the workload increased by 20 $W.min^{-1}$ until the subject could no longer maintain the required power output. The same investigators gave verbal encouragement throughout all maximal tests. Peak power output (PPO) was defined as the highest power output attained during the VO_2max test. Subjects were requested to remain in a seated position for the duration of the MIE and the time trials.

For the measurement of VO_2 during the MIE and the 4-km time trials, subjects wore a mask covering the nose and mouth; the expired air passed through an on-line computer system attached to an automated gas analyzer (Oxycon model Alpha, Mijnhardt, The Netherlands). Before each test, the gas analyzer was calibrated with a Hans Rudolph 5530, 3-L syringe and a span gas mixture. Analyzer outputs were processed by a computer that calculated VO_2 and carbon dioxide production using conventional equations (Jones, 1987). VO_2max was defined as the highest VO2 measured during the MIE.

Heart rate (HR) was recorded every 10 seconds using a Polar Accurex Plus heart rate monitor (Polar Electro.Kempele, Finland). The data were downloaded via an interface into hrm files after completion of the trial. Maximum HR was taken as the highest HR recorded at any stage during the test.

Time-trials

Within seven days of the MIE each subject returned to the laboratory at the same time of day to perform three consecutive 4-km time trials. Successive time trials were separated by approximately 17 min. Subjects were requested to perform the same type of training for the duration of the trial and to refrain from heavy physical exercise for 24 hours before the TT testing.

After a self-selected 10-15 min warm-up, the first TT started after a 2 min countdown during which the cyclists maintained a cycling speed of 35-40 $km.hr^{-1}$. This speed had to remain constant until the start of the time trial. After each time trial, the subjects rested for 10 min after which they performed a 5 min warm-up before commencing the 2 min countdown. Subjects were told to perform each time trial in the fastest time possible but in the knowledge that three trials were to be performed. The elapsed distance was the only feedback given to the subjects during the time trials. They were not informed of completion times until after the final time trial. Power output, HR and VO_2 measurements were recorded continuously during the trials. A fan was positioned in front of the subjects during their time trials and during the 10 min rest interval subjects were allowed to drink water *ad libitum*.

Before the MIE and time trials a 20-gauge Jelco cannula (Critikon, Halfway House, South Africa) was inserted into an antecubital forearm vein for blood sampling. Exactly 3 min (Medbø et al, 1985) after both the VO2max test and each TT, blood was drawn and placed into tubes containing potassium oxalate and sodium fluoride for the measurement of plasma lactate concentration. The blood samples were kept on ice until centrifuged at 3 000 x g for 10 min at 4°C and the plasma stored at -20°C until later analysis. Plasma lactate concentrations were determined by spectrophotometric (Beckman Spectrophotometer -M35) enzymatic assays using the conventional assay (Lactate PAP, bioMérieux Kit, Marcey l'Etoile, France).

Isometric testing of skeletal muscle function

Immediately before the MIE test and time trials, each subject's peak isokinetic force was measured on a Kin-Com isokinetic dynamometer (Chattanooga Group Inc., USA). The peak force produced by the quadriceps muscles was

tested isometrically at an angle of 60°, with full knee extension being the 0° reference.

Subjects performed four 50%, two 70%, one 90% and one 100% familiarization trial of 5 seconds each as a warm-up. After this warm-up each subject performed four 5 second maximal voluntary contractions (MVC) with a 5 second rest between trials. The EMG activity coinciding with the peak torque of the second effort was used to normalise the EMG values recorded during the time trials (Hunter et al, 2002). The subjects were verbally encouraged during the tests to exert a maximal effort.

Electromyographic activity

Muscle recruitment was assessed during the isometric test, as well as during the TTs by measuring EMG activity of the rectus femoris muscle. Electrodes (Thought Technology Triode™ MIEPO1-00, Montreal, Canada) with a bandwidth of 20-500 Hz and sensitivity of < 0.08 μV were attached to the subject's lower limb prior to the start of all testing. The skin overlying the rectus femoris muscle was firstly shaven, after which the outer layer of epidermal cells was abraded with sandpaper and the dirt removed from the skin using an alcohol swab. The triode electrode was placed in the middle of the subject's rectus femoris muscle, secured with self-adherent wrap (Coban 3M, 1582, St. Paul, MN, USA), and linked via a fibre-optic cable to a Flexcomp/DSP EMG apparatus (Thought Technology Montreal, Canada) and host computer. EMG activity was recorded for 5 s during the isokinetic test. During the time trials EMG activity was recorded from 60 to 80 s to coincide with the maximal power output and in 10 s intervals between 200 s to exhaustion during the TTs.

A toggle switch was activated at the beginning of each test to mark the start point of the test procedure, with each activity being sampled at a 1984 Hz

capture rate. A 50 Hz line filter was applied to the raw EMG data to prevent any external interference from electrical sources. The EMG signals from the electrode were band-pass filtered (20-500 Hz) and amplified using standard differential amplifiers (Thought Technology, Montreal, Canada; common mode rejection ratio > 130 dB at 1 kHz, input impedance = 1 million MegOhms, adjustable gain up to 1600). The raw EMG signals were subsequently full wave rectified, movement artefact removed using a high-pass second order Butterworth filter with a cut off frequency of 15 Hz and then smoothed with a low-pass second-order Butterworth filter with a cut-off frequency of 5 Hz. This was performed using MATLAB™ gait analysis software. The integrated EMG data (IEMG) were used for subsequent analyses.

EMG data analysis

All EMG data were normalised by dividing the value at each time point during the cycle trial by the EMG value obtained during the MVC performed before the start of the performance test. Further normalisation of the EMG recorded over the final 90 s of exercise was performed against the mean EMG recorded over the period 60 to 80 s. These data are expressed as a percentage of the mean EMG during the peak power output.

Statistical analysis

Data for HR, VO_2 and power output were averaged over 30 s from 0 to 300 s. EMG data were compared every 10 s from 200 s to fatigue. An analysis of variance was used to assess differences between and within the trials. Once main effects were identified individual differences between the means were located using Tukey's HSD *post hoc* procedure. Significance was accepted at $P < 0.05$. All data are expressed as mean ± standard deviation (S.D.).

Results

Maximum values of VO_2, HR and plasma lactate concentrations

The VO_2max attained during maximal incremental exercise (MIE) was similar to the highest VO_2 measured during each of the 4 km time trials (MIE 71.4 ± 2.3; TT1 70.2 ± 4.1; TT2 70.7 ± 5.3; TT3 69.8 ± 4.2 $mL.kg^{-1}.min^{-1}$) (Figure 1a). Maximum heart rate reached during MIE (193 ± 7 $beats.min^{-1}$) was significantly higher than during TT1 (186 ± 6 $beats.min^{-1}$) and TT2 (187 ± 6 $beats.min^{-1}$) but was not different from TT3 (189 ± 7 $beats.min^{-1}$) (Figure 1b). Post exercise plasma lactate concentrations were similar for all the time trials (TT1 12.7 ± 2.0; TT2 12.8 ± 2.5; TT3 14.0 ± 0.4 $mmol.L^{-1}$) and the concentrations were not different from those observed after the incremental maximal exercise test (14.5 ± 0.8 $mmol.L^{-1}$) (Figure 1c).

Peak and average power outputs

The peak power outputs, reached at 60 seconds (Figure 2a), were significantly higher in the first interval (TT1 556 ± 51 W; TT2 504 ± 44 W; TT3 506 ± 41 W; $p < 0.05$). However, the average power outputs for each interval were not different (TT1 447 ± 30 W; TT2 425 ± 33 W; TT3 434 ± 33 W) (Figure 2b). Nor was the time taken to complete the first interval (284 ± 8 s) and the average velocity (51 ± 1 $km.h^{-1}$) significantly faster than for the third interval (287 ± 9 s and 50 ± 2 $km.h^{-1}$) although it was faster than the second interval (290 ± 9 s and 50 ± 2 $km.h^{-1}$). Completion times were not different between the second and the third interval (Figure 2c). In all trials power output declined significantly from 60 s (Figure 3a) after which it reached a plateau. However, in the second and third intervals the initial increase in power output during the first 30 seconds of exercise was less than in the first trial.

Furthermore, power output rose over the final minute of exercise in the second and third trial (Figure 3a and 4a).

VO_2 and heart rate

The rate of oxygen consumption was similar for all intervals after the first minute (Figure 3b) and did not increase significantly over the duration of the interval. Likewise heart rate did not vary between intervals, but it did increase significantly from the 30th to the 60th second ($p < 0.05$), after which it did not increase significantly (Figure 3c).

iEMG

The iEMG recorded during the period of maximal power output during the time trials was less than 25% of iEMG activity during the MVC (TT1 24.2 ± 3.5; TT1 21.1 ± 4.2%; TT3 23.7 ± 3.8%). There was no difference in iEMG between intervals (Figure 4c). However in all trials iEMG tracked changes in power with the highest values being measured at 60 and 300 seconds when power output was also highest (Figure 4a). Furthermore, iEMG did not increase sequentially across successive intervals and was not higher at 300 seconds than at 60 seconds in any interval.

Discussion

The first important finding of this study was that subjects adopted a similar pacing strategy during each of the three consecutive 4 km intervals (time trials) (Figures 2 and 3) even though they received no external feedback regarding their cycling speeds, power output, duration or heart rates. Distance elapsed was the only external feedback provided.

The pacing strategy adopted was such that the peak power output was reached after 60 seconds where after there was a steep decline in power output, more pronounced in the first interval, so that at 120 seconds, power outputs were the same as in the first 30 seconds. Thereafter power outputs fell only slightly to 240 seconds where after they rose again reaching outputs at 300 seconds that approached those reached after 60 seconds in the second and third trials, but which were lower than the peak values achieved in Trial 1 (Figure 3).

Indeed there was clear evidence of a learning effect since power outputs were higher at 30, 60 and 90 seconds in the first interval, than in the second and third intervals. Thereafter power outputs were essentially the same in all three trials. Thus, the pacing strategies were essentially reproducible throughout the second and third trials. This suggests that subjects may have altered their pacing strategies in the second and third intervals, on the basis of what they learned in the first trial. As a result, performance in the second and third trials was identical. Importantly there was no evidence for the development of a progressive fatigue since power output progressively increased over the last 60 seconds of the final two trials (Figure 4a). Presumably if the faster performance in the first interval had been attempted in the second and third intervals, there might have been the development of a progressive fatigue with a progressive reduction in power output. Rather the finding that the average power output was the same in all three intervals suggests that these cyclists

adopted an ideal pacing strategy for the optimum completion of the total work bout.

Indeed the second important finding of the study was that the power output increased during the final 60 seconds of each time trial, a phenomenon that has also been noted in a longer duration time trials lasting 60 minutes which included six one minute sprint intervals (Kay et al, 2001). These authors also found an increase in iEMG activity and power output to near initial values during the final sprint, following progressive declines in the intervening sprints. If the power output during the time trials had been regulated by peripheral fatigue mechanisms, an increased central neural recruitment of additional motor units would be expected to occur (Crenshaw et al, 1997; Gerdle et al, 1997; Hakkinen et al, 1983; Taylor et al, 1997) in an attempt to compensate for the reduced power output from the fatiguing motor units. This would be shown as a progressive increase in iEMG activity and an irreversibly falling power output. But this did not occur in this study since power output and iEMG changed in parallel during the final 90 seconds of exercise (Figure 4). More significantly, iEMG were not progressively higher in successive time trials as would be expected if peripheral fatigue caused a progressive impairment of the power output of individual motor units, requiring the recruitment of progressively more motor units to compensate for the reduced power output of the fatiguing units.

In addition less than a quarter of the available motor units in the studied muscles were recruited during the time trials, a finding that is consistent with previous observations (Kay et al, 2001; Sjogaard, 1978; St Clair Gibson et al, 2001) but is incompatible with the peripheral fatigue model. For the peripheral model predicts that there must be near total motor unit recruitment at exhaustion so that fatigue results from peripheral metabolite-induced modulation of the contractile activity of all the recruited motor units.

Indeed it is difficult to imagine how peripheral metabolite changes in the skeletal muscles could explain the subtle changes in pacing during the three different intervals. First it seems unlikely that identical metabolite concentrations in the active muscles would explain the identical pacing strategies in the second and third trials. For example, it would seem unlikely that full metabolic recovery could have occurred within 17 minutes after the subjects had already completed 10 minutes of exercise at, or close to, VO_2max. That the plasma lactate concentrations were similar at the end of each interval was unexpected (Figure 1c) and might indicate that a component of the pacing strategy is to complete exercise with specific terminal plasma (and muscle) lactate concentrations (Foster et al, 1994).

Second, since each interval was performed at close to VO_2max, there must have been a progressive increase in plasma and muscle lactate concentrations during each interval. If a progressive rise in the muscle lactate concentrations impairs exercise performance, then the athletes should have shown a pacing strategy that produced a maximum power output in the first seconds of exercise with a progressive fall thereafter with the lowest power outputs in the last seconds of each interval, most especially in the last interval. As already described, this did not occur (Figure 3a).

Rather, the most plausible explanation is that the pacing strategy results from changes in the number of motor units that are alternatively recruited and de-recruited during different stages of exercise. This would occur if a subconscious "controller" determines the overall pacing strategy during exercise by matching the rate of energy expenditure and the current energy reserves with the predicted energy cost of the exercise (Ulmer, 1996), but within the physiological capacity of the individual. Ulmer (1996) was perhaps the first to propose that the optimal metabolic rate during exercise is maintained by the action of a programmer that takes cognisance of the

duration or distance, or both, of the planned effort and calculates the optimum pacing strategy on the basis of previous experience. This pre-emptive mechanism would not only pattern a single time trial, but would be responsible for the pacing strategy adopted in the consecutive trials that comprise the entire exercise bout.

The third noteworthy finding of the study was that despite the different power output profiles (Figure 3a) between the first and third intervals, the average velocities were quite similar as were the finishing times. Foster et al (1994) have postulated the presence of a central mechanism governing muscle recruitment that is influenced by afferent sensory feedback of pH levels in the exercising muscle. They suggest that athletes learn to 'sense' the intramuscular pH and adapt their workload on the basis of this feedback so that a critically low muscle pH is never approached.

The proposed mechanistic functioning of this feedback system involves the detection of pH changes by nociceptors or chemoreceptors that transmit an inhibitory signal to the central nervous system, which is perceived as a "sensation". As a result, the motor cortex decreases efferent neural drive directed to those motor units in the exercising muscles from which the afferent signals were received. The degree of reduction in efferent activity is proportional to the magnitude of afferent feedback activity. Therefore, a centrally directed pacing strategy is adopted, which is fine-tuned in the motor cortex in response to this peripheral feedback.

The lag phase inherent in this model would explain the power output profile observed in the first time trial in which there was an initial very rapid increase in power output with a disproportionably large percentage of the total work performed in the initial stages of exercise. However, in the third time trial the initial spike in power output is dampened, which is consistent with the

peripheral monitoring theory proposed by these workers (Foster et al, 1994) since it is unlikely that complete intramuscular biochemical homeostasis, would have been restored during the rest periods between trials (Busse et al, 1989). Alternatively this modification could have resulted from changes in feedforward control as a result of information acquired during the first interval. Although muscle pH and lactate may act as the monitored chemicals, neither would appear to be limiting factors according to those studies that have dissociated blood lactate concentrations and pH from changes in performance (Schabort et al, 2000) by altering blood lactate and pH during stochastic 40 km time trials without equivalent changes in performance. Similarly Medbø and Sejersted (1985) concluded that blood lactate concentrations do not limit physical performance during exhaustive exercise.

In summary, this study shows that the pacing strategies adopted by athletes during 3 successive 4km cycling time trials that each elicited a VO_2 max response were remarkably similar, despite the absence of external feedback to the subjects other than distance covered. Importantly, power outputs and iEMG activities rose progressively and similarly from 210 – 300 seconds of exercise in all three intervals. The finding that the pacing strategies were remarkable similar, that iEMG activities were not progressively greater in successive intervals and that only about 25% of available motor units were recruited at the point of peak power output, suggests the presence of a centrally-determined, anticipatory regulation of the adopted pacing strategies. Such regulation would result from a centrally-determined recruitment and de-recruitment of more or less motor units during the exercise bout. The extent to which the pacing strategy is influenced by feedback from metabolic events in the active muscles could not be determined by this study.

TABLE 1

Subject characteristics and results from the maximal incremental exercise test (n=7)

Age (yr)	23.7 ± 4.4
Height (m)	1.81 ± 0.09
Mass (kg)	73.7 ± 9.2
VO_2max ($mL.kg^{-1}.min^{-1}$)	71.4 ± 2.3
HRmax ($beats.min^{-1}$)	193 ± 7
PPO (W)	463.6 ± 32.4
P:W ($W.kg^{-1}$)	6.3 ± 0.6
La_{peak} ($mmol.L^{-1}$)	14.5 ± 0.8

Values are expressed as mean ± SD

VO_2max peak oxygen uptake

HRmax maximum heart rate

PPO peak power output

P:W power to weight ratio

La_{peak} peak blood lactate

Figure 1 Mean maximum values of VO_2, heart rate and lactate concentrations attained during the maximal incremental exercise and three consecutive 4 km time trial intervals.

Figure 2 Peak power output, mean power output and the performance time for the three consecutive 4 km time trial intervals.

λ 1st interval is significantly different from the 2nd and 3rd intervals ($p < 0.05$)

* 2nd interval is significantly different from the 1st interval ($p < 0.05$)

Figure 3 Power output, VO_2 and heart rate for the duration of the consecutive 4 km time trial intervals.

a 1st interval is significantly different from the 2nd and 3rd intervals ($p < 0.05$)

b Significantly different from 60 s in the 1st interval ($p < 0.05$)

c Significantly different from 60 s in the 1st and 2nd intervals ($p < 0.05$)

d Significantly different from 60 s for all intervals ($p < 0.05$)

e Significantly different from the 2nd interval ($p < 0.05$)

Figure 4 Absolute power, relative power and relative iEMG at 60, 210, 240, 270 and 300 s in each of the three consecutive 4 km time trials.

a 1st interval is significantly different from the 2nd and 3rd intervals ($p < 0.05$)

b Significantly different from 60 s in the 1st interval ($p < 0.05$)

d Significantly different from 60 s for all intervals ($p < 0.05$)

FIGURE 7

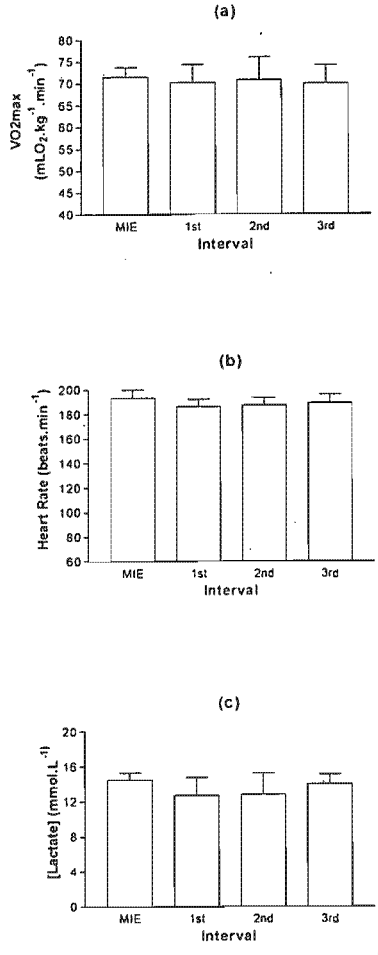


FIGURE 2

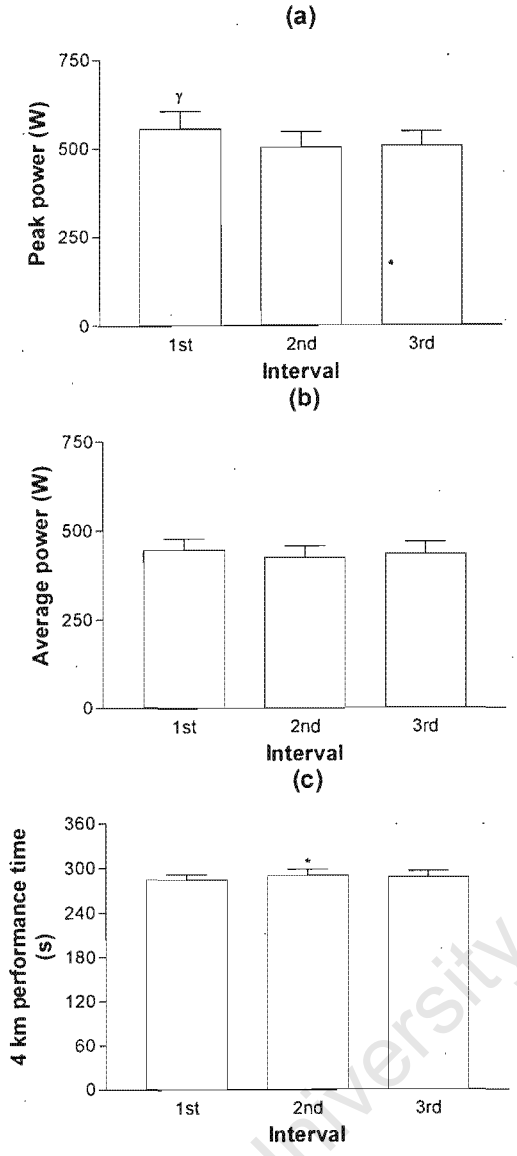


FIGURE 3

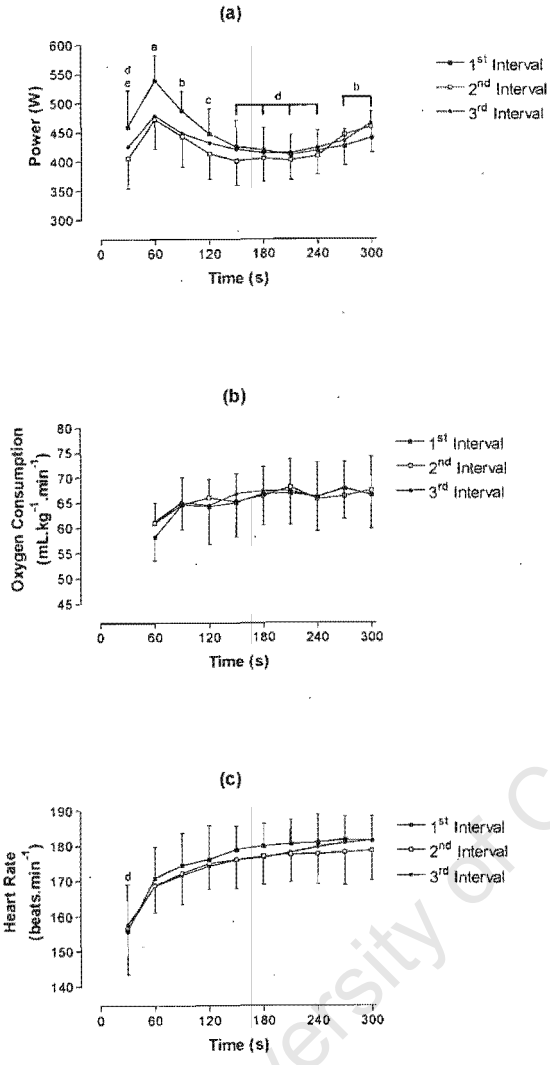
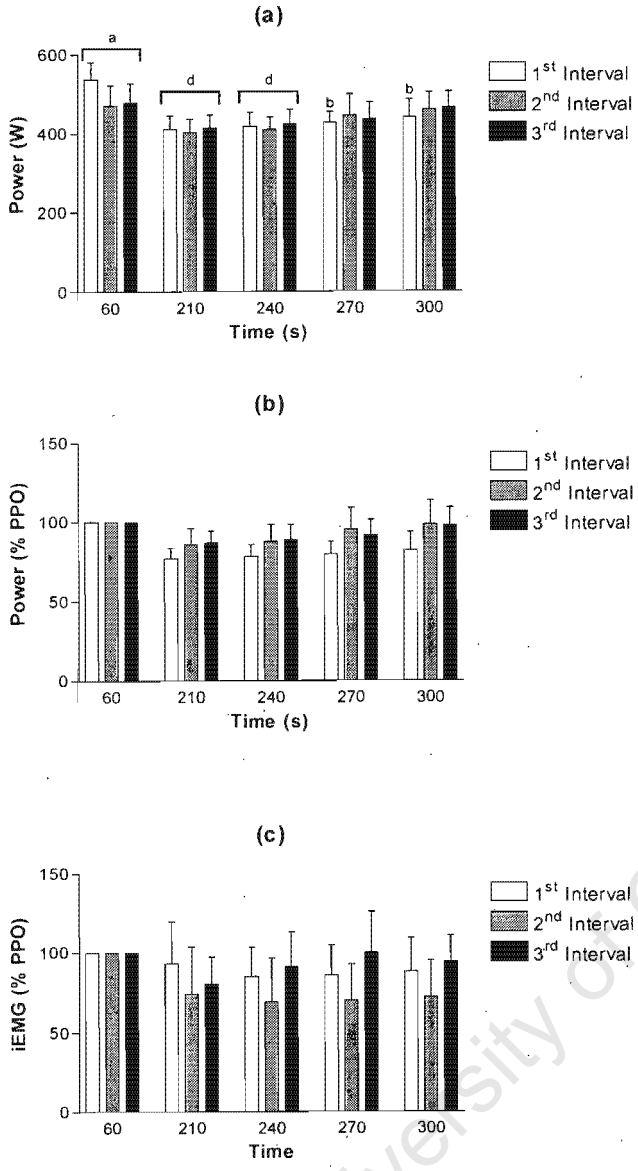


FIGURE 4



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IV) PHYSIOLOGICAL EFFECTS OF TWO LEVELS OF HYPEROXIA DURING MAXIMAL EXERCISE IN A PRESSURE-SEALED CHAMBER

Introduction

Studies by AV Hill and his colleagues in the 1920's laid the foundation for the classical theory that skeletal muscle anaerobiosis limits the maximal exercise capacity of humans (Hill et al, 1925) and other athletic mammals (Hodgson et al, 1990; Mason, 1998; McMiken, 1983; Schuback et al, 1999).

Supportive evidence for this theory comes from studies showing that interventions that increase oxygen delivery to the active muscles including the use of erythropoietin (Birkeland et al, 2000) or autologous blood reinfusion (blood doping) (Gledhill, 1982) increase both exercise performance and maximal oxygen consumption (VO_2max).

Stimulated by the original proposal of A.V. Hill and colleagues that a "governor" may exist in either the heart or brain, specifically to insure that myocardial damage does not develop during maximal exercise (Hill et al, 1925), we have extended the original hypothesis by proposing the existence of this "central governor" in the brain (Noakes et al, 2001; St Clair Gibson et al, 2001). The function of the postulated central governor is to limit the number of motor units that can be recruited during maximal exercise, specifically to ensure that neither anaerobiosis nor ischemia of the heart, exercising muscles or brain can occur. This theory predicts that in response to impending hypoxia or ischemia of any of these organs, afferent sensory feedback information to the "central governor" will prevent the recruitment of additional motor units in the exercising muscles (Noakes et al, 2001), thereby preventing that further increase in work rate and hence whole body oxygen consumption that would produce tissue damage.

Findings consistent with the action of this postulated governor include the absence of myocardial ischemia during any form of maximal exercise in

healthy humans (Raskoff et al, 1976) even when they exercise in profound hypoxia at extreme altitude equivalent to the summit of Mount Everest (Groves et al, 1987; Suarez et al, 1987; Sutton et al, 1992; West et al, 1983). Furthermore, motor unit recruitment (Kayser et al, 1994), blood lactate concentrations (Hochachka et al, 2002) and cardiac output (Peltonen et al, 2001), are all lower during maximal exercise at high altitude or hypoxia than at sea level or in normoxia, consistent with the theory that exercise in hypoxia is regulated by a central brain governor specifically to ensure that the extent of motor unit recruitment is never sufficient to produce profound arterial desaturation and hypoxic tissue damage (Noakes et al, 2001).

This hypothesis also predicts that exercise in hyperoxia should produce physiological responses opposite to those measured in hypoxia, in particular increased motor unit recruitment, a higher peak work rate and elevated VO_2max compared to maximal exercise in normoxia. Whilst a number of studies of maximum exercise in hyperoxia have been reported, the results are inconsistent, raising questions about either the accuracy of the research methods or of the validity of these physiological theories.

Thus whereas the earliest studies (Furasawa, 1925; Hill et al, 1924) reported that hyperoxia increased the VO_2max by up to 50%, more modern studies have found substantially more modest increases from 2 – 20% (Adams et al, 1980; Davies et al, 1974; Ekblom et al, 1975; Welch et al, 1974; Welch et al, 1981; Weltman et al, 1978). with some failing to show even any effect of hyperoxia on either VO_2max or maximal exercise performance (Hogan et al, 1983; Plet et al, 1992).

Technical considerations that may have influenced these results and their interpretation include the wide range of inspired oxygen fractions (F_IO2) used to produce hyperoxia; the small number of studies that have compared the

effects of a range of different FiO_2 (Welch, 1982); and the possibility that measurement errors can cause the VO_2max to be overestimated in hyperoxia, either because the Douglas Bag technique is used (Welch et al, 1981) or because modern automated systems for measuring VO_2 may produce erroneous results when the inspired F_IO2 is beyond the physiological range (Hornby et al, 1995). In addition, the usual method for altering F_IO_2 requires that the athlete inhale the different gas mixture through variable lengths of respiratory tubing that lead from the large mixing bags used to produce inspiratory gas mixtures with different F_IO_2. This contrasts with the usual system in which the athlete inhales room air, through a single low resistance valve.

Our preliminary studies raised the possibility that subjects who inhaled gasses from such a mixing bag system complained of increased perceptions of dyspnoea and appeared to terminate exercise prematurely as a result of an increase in the perceived work of breathing. Peak ventilation rates were also lower when subjects inhaled room air from the mixing bag system than when they inhaled air without passage through the additional respiratory tubing. Indeed it is known that increasing the resistance to inspiratory airflow can significantly impair exercise performance (Dressendorfer et al, 1977).

Accordingly, the aim of this study was to re-evaluate the effects of three different levels of F_IO_2 on maximal exercise performance, maximal rates of ventilation, VO_2max and parameters of arterial oxygen content in conditioned subjects who inhaled all the gas mixtures, including room air, directly from the surrounding environment. Thus the novel innovation in this study was that subjects exercised in a sealed pressure chamber, the oxygen partial pressure of which was maintained constant by the continual addition or removal of the appropriate gasses. This ensured that inspiratory and expiratory airflow

resistance was minimised and identical for all test conditions. By excluding any possible influence of the additional inspiratory resistance produced by the delivery systems usually used to provide inspiratory gasses with different F_IO_2, we were able to isolate any direct effects of altered F_IO_2 on exercise performance and other physiological variables during progressive maximal exercise to exhaustion. We theorised that increasing F_IO_2 would produce a dose-related increase in VO_2max and maximum work rate consequent to increased arterial oxygen content and hence increased capacity to transport oxygen to oxygen-sensitive organs.

Methods

Subjects

Eight subjects were recruited for this study, which was approved by the Research and Ethics committee of the Faculty of Health Sciences of the University of Cape Town. The nature of the study, including the risks associated with arterial sampling, was carefully explained, after which informed consent was obtained from each subject prior to the start of testing.

Experimental protocol

Each subject was required to perform an incremental ramp cycle test to exhaustion on a Lode cycle ergometer (Excalibur, Netherlands) on three separate occasions, whilst breathing air with F_IO_2 of 21 (room air), 35 or 60%. Consecutive tests were separated by at least 3 but not more than 14 days. Tests were performed at the same time of day and the testing order was randomised and single-blinded since the experimenter but not the subject was aware of the F_IO_2 to be produced inside the pressure chamber. The cycle ergometer ramp protocol consisted of a 2 min warm-up ride at 150W. Thereafter, the workload of the ramp protocol increased by 0.5W.sec^{-1} until the subject volitionally terminated the exercise.

All tests were performed in the pressure sealed chamber that was pre-filled with either room air or 35 or 60% O_2 depending on the trial to be performed. The chamber was not pressurised for any test and the oxygen concentration was readjusted once the subject and researcher had entered the chamber. Typically, the F_IO2 did not drop more than 1 or 2% whilst the chamber door was opened to allow entry to the subject and researcher. The appropriate F_IO_2 was usually achieved within two minutes of resealing the chamber door.

Prior to each test, subjects sat quietly for 10 minutes in the chamber while breathing the relevant gas mixture to ensure adequate equilibration of the new gas mixture in all body compartments and also complete mixing of the new gas mixture throughout the pressure sealed chamber.

Pressure sealed (Hyperbaric) Chamber

The subjects cycled inside a Multi-place Class "A" 18 000 L pressure sealed chamber of length 3.5 m and diameter 2.5 m built to Lloyd's and ASME 1 PVHO specifications. There were internal CO_2 scrubbers and O_2, temperature and humidity were continuously monitored. Two oxygen sensors in different areas of the chamber continuously monitored the ambient oxygen fraction. When the FiO_2 dropped 2% below the required percentage, oxygen was fed into the chamber until the requisite level was again achieved.

Blood Sampling

A 20G Jelco™ cannula was inserted into the subject's radial artery 5 minutes before he entered the chamber. The first (resting) blood sample was drawn after the subject had rested in the chamber for 10 minutes to ensure complete equilibration of the new FiO_2. Thereafter arterial blood was sampled every three minutes during the trial. During each sampling, 2 ml of blood was drawn into a vacutainer tube containing potassium oxalate and sodium fluoride for the measurement of plasma lactate concentrations. Another 2 ml was drawn into a Radiometer PICO™ 50 blood gas aspirator (Copenhagen, Denmark) for blood gas analysis.

Blood Analyses

Blood gas concentrations and pH

Arterial blood gas samples were stored on ice and analysed within 30 min. Analysis for partial pressure of oxygen (pO_2) and carbon dioxide (pCO_2); pH; oxygen saturation (sO_2); and haemoglobin oxygen saturation (O_2Hb) was performed by a Radiometer ABL 505 (Copenhagen, Denmark) coupled to a Radiometer OSM3 (Copenhagen, Denmark).

Lactate

Blood samples for lactate analysis were stored on ice until centrifuged at 3000 x g for 10 min at 4°C and the plasma stored at -20°C. Plasma lactate concentrations were determined by spectrophotometric (Beckman Spectrophotometer – M35) enzymatic assays using a lactate kit (Lactate PAP, bioMérieux Kit, Marcey l'Etoile, France).

Expired respiratory gas analyses

For the measurement of VO_2, CO_2 production and minute ventilation (V_E), subjects wore a mask covering the nose and mouth and inhaled air directly from the chamber across a single low resistance valve. The expired air passed over a hot wire anemometer to determine ventilatory volume and a sample was drawn through an on-line, breath-by-breath gas analyser (Vmax 229 Series, Sensor Medics, California). Before each test the pneumotachograph was calibrated with a Hans Rudolph 5530, 3L syringe and the gas analyser by span gases composed of 25.8% O_2: 0% CO_2 and 15.6% O_2: 4.1% CO_2. Oxygen consumption and CO_2 production were calculated using conventional Haldane equations and averaged over 30 seconds. Maximum oxygen consumption (VO_2 max) was defined as the highest VO_2 measured during the test.

Criteria for identifying the "plateau phenomenon" in oxygen consumption

To determine the incidence of individual plateau phenomena, we adopted the historical methods of Taylor et al (1955). The mean increase in VO_2 across two consecutive 30 s periods from 240 s to 90 s preceding fatigue at 0 s was determined and we defined the criterion for a plateau in VO_2 in this particular testing protocol as any rate of increase in VO_2 less than 50% of the normal rate of rise in oxygen consumption. In order to avoid the error of describing a false plateau where none existed (Glassford et al, 1965), for the achievement of a true "plateau phenomenon", subjects were required to exhibit an increase in VO_2 of less than the mean increment across two consecutive 30 second periods.

Heart rate

Heart rate (HR) was recorded every 10 seconds using a Polar Accurex Plus heart rate monitor (Polar Electro.Kempele, Finland). The data were downloaded via an interface into hrm files after completion of the trial. Maximum HR was taken as the highest HR recorded at any stage during the test.

Statistical analyses

Data for submaximum VO_2, VCO_2, V_E and power output were averaged over 30 s from 0 to 330 s for all subjects to avoid the confounding effect of subject dropout, which began after 330 seconds of the test. For the comparison of VO_2, VCO_2 and V_E during the final minutes of exercise immediately preceding fatigue, data were averaged for 30 s intervals, backwards from the point of fatigue. For maximum and submaximum data, a repeated measures Analysis of Variance was used to assess differences between and within the

trials. Once main effects were identified, individual differences between the means were located using Fischer LSD *post hoc* procedure. Significance was accepted at $P < 0.05$. All data are expressed as mean ± standard deviation (S.D.).

Results

Partial pressure of oxygen (pO_2)

The arterial pO_2 values were significantly different between trials at all time points, also showing a dose-dependant response to increases in F_IO_2 (Table 1). The pO_2 fell during exercise in normoxia and was also lower at fatigue than at rest during exercise in 35% O_2. In contrast, pO_2 rose throughout exercise with F_IO_2 of 60%.

Partial pressure of carbon dioxide (pCO_2)

Arterial pCO_2 rose from rest to 3 min where after it stabilised except in F_IO_2 21% when it fell at exhaustion (Table 1). Altering the F_IO_2 did not significantly alter the arterial pCO_2, although values at fatigue were higher at F_IO_2 of 35 and 60%.

pH and lactate

The pH decreased and lactate concentrations increased progressively during the trials but were not different between trials (Table 1).

Oxygen saturation (sO_2)

The arterial sO2 was higher at all times during exercise and at exhaustion in both hyperoxic conditions than in normoxia. Oxygen saturation decreased significantly during exercise with F_IO_2 of 21% whereas it exceeded 99% in both hyperoxic trials at both rest and throughout exercise (Table 1).

Haemoglobin saturation (O_2Hb)

Haemoglobin saturation was significantly higher in both hyperoxic trials than in normoxia. Whereas O_2Hb fell during exercise with F_IO_2 of 21%, it remained unchanged during exercise in both hyperoxic conditions (Table 1).

Maximum values of VO_2, VCO_2, V_E, HR and power output

The VO_2max was significantly increased in exercise with F_IO_2 of 35 (5.2 ± 0.6 L.min^{-1}) or 60% (5.2 ± 0.7 L.min^{-1}) compared to 21% (4.8 ± 0.5 L.min^{-1}; $p < 0.05$) (Figure 1) but was not significantly different between the hyperoxic conditions. Neither the peak rates of CO_2 production (21% = 5.9 ± 0.7 L.min^{-1}; 35% = 6.1 ± 0.7 L.min^{-1}, 60% = 6.0 ± 0.6 L.min^{-1}), maximal minute ventilation (21% = 160 ± 21 L.min^{-1}, 35% = 162 ± 30 L.min^{-1}, 60% = 154 ± 27 L.min^{-1}) (Figure 1) nor maximal heart rates (21% = 186 ± 6 beats.min^{-1}, 35% = 190 ± 7 beats.min^{-1}, 60% = 188 ± 9 beats.min^{-1}) were influenced by the F_IO_2. Peak power output was also not influenced by F_IO_2 (21% = 373 ± 28 W, 35% = 374 ± 28 W, 60% = 382 ± 39 W) (Figure 1).

However, a more careful analysis of the individual responses to hyperoxia revealed that two subjects performed worse in both hyperoxic trials than in normoxia (Subjects 2 and 7, Figure 2). Although these subjects were trained athletes, they were the only two subjects who were not trained in the activity, cycling, that was the chosen testing mode in these trials. Nor were they as familiar with the testing protocols as the other subjects. Thus of the 16 tests in hyperoxia, the peak work rate increased in 10 and was the same or reduced in the remaining six tests. Subjects 2 and 7 performed worse in both the hyperoxia trials, comprising four of the six trials in which hyperoxia did not improve exercise performance. There is no known physiological mechanism by which hyperoxia impairs athletic performance. When their data were

cluded from analysis, the data for the remaining 6 subjects showed an crease in maximum work rate at F_IO_2 of 35% (379 ± 30 W; $p = 0.4$) and a gnificant increase in peak work rate in F_IO_2 60% compared with 21% (391 ± W vs. 374 ± 32 W; $p < 0.02$). Peak work rate was however not significantly fferent between the two hyperoxic conditions.

ubmaximum values

O_2 rose as a linear function of work rate in all trials (Figure 3; top left panel). rthermore, VO_2 for the first six minutes of the trials was significantly higher both the hyperoxic trials than in normoxia. The mean VO_2 for the final six nutes of exercise was significantly higher for 35% (4.31 ± 0.75 $L.min^{-1}$) and % (4.42 ± 0.79 $L.min^{-1}$) trials than for 21% F_IO_2 (4.05 ± 0.79 $L.min^{-1}$) gure 4; top left panel). Carbon dioxide production, minute ventilation and art rate rose similarly in all three trials with a clearly exponential rise in nute ventilation in the last 180 seconds of exercise (Figure 4). Since bmaximal VO_2 increased but VCO_2 production was unchanged, RER was duced in the first 300 (Figure 3) and final 360 (Figure 4) seconds of both peroxic trials, although the reduction was not significant.

cidence of the "plateau phenomenon" in oxygen nsumption

O_2 rose linearly during the first six (Figure 3) and final five minutes (Figure of exercise without any evidence for a "plateau" in VO_2 except, perhaps, ring the 60% F_IO_2 trial (Figure 4). To determine the incidence of individual teau phenomena, we adopted the historical methods of Taylor et al (1955) aylor et al, 1955). The mean increase in VO_2 across two consecutive 30 s iods from 240 s to 90 s preceding fatigue at 0 s (Figure 4), was 179 $L.min^{-1}$, which is similar to the values obtained in previous studies (Barstow

et al, 1996; Walsh et al, 1995). Accordingly we defined the criterion for a plateau in VO_2 in this particular testing protocol as any rate of increase in VO_2 less than 50% of the normal rate or less than 90 $mL.min^{-1}$ across two 30 s consecutive periods. In order to avoid the error of describing a false plateau where none existed (Glassford et al, 1965), for the achievement of a true "plateau phenomenon", subjects were required to exhibit an increase in VO_2 of less than 90 $mL.min^{-1}$ across two consecutive 30 second periods. According to these criteria, a plateau in VO_2 was only exhibited by a single (different) subject in each condition; that is only three of 24 tests (13%). The mean change in VO_2 for subjects who did not exhibit a plateau in oxygen consumption for the final 60 s of all the trials was 340 ± 210 $mL.min^{-1}$ whereas in the subjects for whom plateaus in VO_2 were identified, there was a fall in VO_2 of –150 ± 190 $mL.min^{-1}$. However, the three subjects who developed the plateau phenomenon achieved higher VO_2max values in at least one of the other tests in which the plateau phenomenon did not develop. Thus VO_2max values during the "plateau test" in these subjects was 4.5 ± 0.7 $L.min^{-1}$, whereas the VO_2max during a "non-plateau" test was 4.9 ± 0.5 $L.min^{-1}$.

Discussion

Exercise in hyperoxia with an F_IO_2 of either 35 or 60% produced a significant increase in arterial pO_2, percent arterial O_2 saturation and percent haemoglobin saturation (Table 1). Furthermore, whereas arterial pO_2, percent arterial O_2 saturation and percent haemoglobin saturation fell during exercise with F_IO_2 of 21%, they remained elevated during exercise with F_IO_2 of either 35 or 60% (Table 1). Arterial pO_2 was also significantly higher during exercise with F_IO_2 of 35% or 60% but percent haemoglobin saturation and percent arterial O_2 saturation were not different between the different hyperoxic conditions.

Accordingly, our first conclusion was that exposure to hyperoxia produced the expected alterations in arterial oxygen content and that only the increase in pO_2 was greater during exercise with an F_IO_2 of 60 than with 35%. Furthermore, maximal exercise in hyperoxia prevented any fall in pO_2 during exercise although the fall in normoxia was small. Percent arterial saturation remained above 99% in hyperoxia. Thus the methods for inducing hyperoxia were effective and induced a dose-dependant increase in arterial pO_2. In contrast, the increase in percent arterial O_2 saturation and in percent haemoglobin saturation was maximised in F_IO_2 of 35% and did not increase further in F_IO_2 of 60%.

Our second finding was that the submaximal VO_2 as well as the VO_2max was increased during exercise with F_IO_2 of 35 or 60%. However, VO_2max was not significantly higher in F_IO_2 of 60% than with 35% F_IO_2.

The finding that VO_2max increased significantly during maximal exercise in hyperoxia (Figure 1) is common to the majority (Knight et al, 1993; Richardson et al, 1999; Welch et al, 1974; Weltman et al, 1978) but not all

(Adams et al, 1980; Hogan et al, 1983; Hughson et al, 1995) previous studies. The magnitude of the increase of ~8% measured in this study was, however, substantially less than the unphysiologically large increases of up to 50% reported in the earliest studies but was similar to the more modest increases of 2 – 20% reported in the majority of more modern studies (Byrnes et al, 1984; Richardson et al, 1999; Welch et al, 1974; Weltman et al, 1978).

The increase in submaximum VO_2 in hyperoxia (Figures 3 and 4) is a consistent finding in the majority of studies (Welch et al, 1974; Weltman et al, 1978) and has been attributed to changes in O_2 saturation of arterial blood delivered to the tissues, which alters the circulatory and diffusion dynamics resulting in an increase in O_2 uptake (Wagner, 1991) since VO_2 increases but VCO_2 remains unaltered in hyperoxia, RER was reduced throughout exercise (Figures 3 and 4) implying that fat metabolism was stimulated and carbohydrate oxidation suppressed by hyperoxia (Adams et al, 1986).

What is less easy to understand is the physiological value of the increase in submaximum VO_2 in hyperoxia. For any increase in submaximum VO_2 would usually be interpreted to indicate an impaired efficiency of movement as reported by Walsh and Banister (1995). It is difficult to conceive how a simple increase in F_IO_2 would cause this to happen. Alternatively, any biochemical explanation requires there to be a relative inhibition of oxygen consumption in some tissues during exercise in normoxia, which is also difficult to conceptualise.

Another possibility is that measurement error might explain an overestimation of the real VO_2 during exercise in hyperoxia. Many different systems including mass spectrometry have been used to measure VO_2 in hyperoxia and these have usually shown an increase in both submaximum and maximum VO_2 in hyperoxia. We also used a state-of-the-art system to measure VO_2 in

hyperoxia but the finding that only VO_2 but not VCO_2 was increased; the absence of a logical physiological explanation for the finding, in particular why movement economy should be impaired, carbohydrate oxidation suppressed and fat metabolism stimulated in hyperoxia; and the historically known difficulty in measuring VO_2 in hyperoxia (Hornby et al, 1995; Welch et al, 1981), leads us to suggest that perhaps even state-of-the-art modern systems for respiratory gas analysis may be unable to measure VO_2 accurately in hyperoxia. More sophisticated gas analysis systems may be necessary in future to resolve this question.

This interpretation has important consequences since it is a common practice to measure changes in the VO_2max as a surrogate for changes in performance on the assumption that the two measurements are causally related (Basset et al, 2000). However, in this study, although the VO_2max of the total group increased significantly, peak work rate of the total group did not increase in hyperoxia (Figure 1) indicating a discrepancy between the increase in VO_2max and peak work rate in hyperoxia. Others have also observed that there is a marked discrepancy in the magnitude of the increase in VO_2max and in peak work rate in hyperoxia (Welch, 1982), again raising the question of a measurement error in VO_2max.

But a more careful individual analysis of the peak work rates in hyperoxia indicated that maximum exercise performance of two subjects who were not habituated to cycling, was impaired in both hyperoxic conditions (subjects 2 and 7 in Figure 2). Exclusion of their data on the grounds that there is no known physiological explanation for a consistent impairment of exercise performance by hyperoxia, revealed that peak work rate was increased in the remaining six subjects at F_IO_2 of 35% ($p < 0.4$) and significantly increased at an F_IO_2 of 60% ($p < 0.02$). Accordingly we conclude that the small numbers

of subjects in this study may have caused the false negative findings that the peak work rate did not increase in hyperoxia.

Thus the findings of this study are more likely to support rather than refute the majority finding that peak work rate is increased in hyperoxia (Adams et al, 1980; Hughson et al, 1995; Knight et al, 1993; Peltonen et al, 1997; Wilson et al, 1975). However, the effect of hyperoxia on maximum performance is relatively quite small and, as this study suggests, may require well-trained athletes habituated to the testing protocols to produce a consistently measurable effect.

Our fourth finding was that exposure to hyperoxia altered neither submaximum (Figure 3) nor maximum V_E (Figure 1 and 4) as previously reported (Adams et al, 1980; Hesse et al, 1981; Knight et al, 1993; Welch et al, 1974). This must indicate that feedback from arterial O_2 sensors is not a major determinant of V_E during exercise in normoxia. Rather, feedforward control or linkage of V_E to rates of CO_2 production or to the external work rate via afferent sensory feedback from the exercising skeletal or respiratory muscles may be involved. We have previously shown that V_E appears to be linked to the rate of carbohydrate oxidation both before and after physical training (MacRae et al, 1995). If this is indeed correct then the apparent reduction in RER in hyperoxia (Figures 3 and 4) should have reduced V_E in this study. Since it did not, either the rate of carbohydrate oxidation is not a determinant of V_E or, as we suspect, the RER was not accurately measured in hyperoxia in this study.

Our fifth finding was that hyperoxia also did not alter either the pH or lactate response (Table 1) to progressive maximal exercise, as also found in the majority of previous studies (Adams et al, 1980; Knight et al, 1993; Peltonen et al, 1997). It is usually presumed that hyperoxia acts by increasing oxygen

delivery to the exercising muscles, thereby delaying the onset of anaerobiosis and the development of the limiting muscle pH and lactate concentrations that impair skeletal muscle contractile function, inducing fatigue and the termination of exercise. Since neither arterial pH nor lactate concentrations were altered even during exercise in F_IO_2 of 60%, this explanation appears unlikely. Indeed exercise terminated at arterial pH concentrations well above those that have been shown to impair skeletal muscle contractile function in vitro (Shee et al, 1990; Westerblad et al, 1988).

Furthermore, during exercise with an F_IO_2 of 60%, the increase in O_2 saturation of the blood and haemoglobin increased the O_2 available to the periphery by approximately 400 $mL.min^{-1}$ according to conventional equations (McArdle et al, 1991). Based on the oxygen cost of the ramp protocol, this translates into an increased workload of over 30 W (60 s exercising time). However, in actuality, the subjects only managed to increase their work output by ~10 W, indicating either a measurement error, or that movement efficiency was altered in hyperoxia, or that there was excess O_2 consumption, superfluous to that needed to produce an increase in work rate. Alternatively, if the VO_2 was correctly measured, then the development of an oxygen deficiency could not explain the termination of maximum exercise in normoxia, since an increase in VO_2max in the total group did not increase the maximum work rate in hyperoxia.

Further evidence that hyperoxia in this experiment was unlikely to act purely by increasing oxygen delivery to the exercising muscle was found by the presence of the so-called "plateau phenomenon" in 13% of the maximal tests.

We have described elsewhere (Noakes, 1988; Noakes, 1997; Noakes, 2000) that the "plateau phenomenon" provides the sole historical basis for the theory that an oxygen deficiency limits maximal exercise performance by

inducing skeletal muscle anaerobiosis and metabolite-induced inhibition of skeletal muscle contraction, according to the peripheral fatigue model interpretation from the observations of A.V. Hill and his colleagues. Hence, according to that theory, the "plateau phenomenon" should always be present at the termination of exercise and hyperoxia should act by increasing the work rate at which the inevitable "plateau phenomenon" develops, thereby also delaying the achievement of limiting muscle and blood lactate concentrations and acidic pH.

Indeed, the incidence of the "plateau phenomenon" in this study (13%) is the lowest yet reported in this literature. Since the plateau phenomenon did not occur in five of the eight subjects in any of their trials it must be assumed that, according to the traditional theory (Hill et al, 1924; Taylor et al, 1955), none of those subjects stopped exercising because of an oxygen deficiency in their exercising muscles, as traditionally described. Furthermore since the phenomenon occurred only once in the three tests in three different individuals all of whom attained a higher VO_2max in another trial, it seems highly improbable that this is a reproducible physiological phenomenon, whose significance is fully understood (Myers et al, 1989; Myers et al, 1990). But, if an oxygen deficiency in the active muscles seems an unlikely explanation for why these subjects stopped exercising, especially in hyperoxia, the question remains: What physiological cues caused the subjects to stop exercising at the VO_2max?

Variables that were the same at exhaustion in all conditions and which might therefore have acted as physiological cues for exhaustion were pCO_2, pH, lactate (Table 1) and rates of CO_2 production and ventilation (Figure 4). The four metabolic variables are inter-related and hence difficult to differentiate. The maximum rate of ventilation is usually considered a potentially limiting

factor for maximum exercise since it may limit the degree of arterial oxygenation.

However, in this experiment, the same peak rates of ventilation produced different degrees of arterial oxygenation (Table 1) and hence, potentially, different rates of muscle O_2 delivery. This raises the alternate possibility that the muscular effort involved in producing a maximal V_E might be part of the afferent sensory input to a central governor that determines the point at which exercise terminates. This would act similar to the J reflex identified in animals and which is evoked by the activation of pulmonary C fibres. The J reflex causes the inhibition of skeletal muscle recruitment and the limitation of exercise in animals (Gandevia et al, 2000). However, recent studies have shown that the activation of C fibres in humans causes respiratory discomfort alone (Gandevia et al, 2000).

In summary, this study found that exercise in hyperoxia with F_IO_2 of either 35 or 60% significantly increased arterial pO_2 in a dose-dependant response and maintained pO_2, sO_2 and O_2Hb during exercise. As predicted by both the central governor (Noakes et al, 2001) and the A.V. Hill Cardiovascular/Anaerobic models of exercise physiology (Noakes, 2000), hyperoxia significantly improved both peak work rate and the VO_2max in the 6 habituated cyclists who were studied. However the effect on exercise performance (~10 W) was less than that expected from the increase in VO_2max and was not significantly greater in F_IO_2 of 60% than in 35%.

More importantly, there was little evidence to support a conclusion that this effect of hyperoxia was due solely to increased peripheral O_2 delivery and the prevention of skeletal muscle anaerobiosis. First, the incidence of the "plateau phenomenon" – the traditional gold standard for the development of skeletal muscle anaerobiosis (Basset et al, 1997; Hill et al, 1924) - was the lowest (13%)

yet reported in any published study. Thus according to the explanation based on the traditional hypothesis, the low prevalence of this phenomenon shows that at least 87% of all tests were not limited by the development of skeletal muscle anaerobiosis. Hence hyperoxia could not have improved exercise performance by offsetting skeletal muscle anaerobiosis in those 87% of maximal tests that were not terminated by the development of skeletal muscle anaerobiosis in normoxia. Indeed in those three tests in which a "plateau phenomenon" was identified, subjects reached higher VO_2max values in subsequent tests. Second, hyperoxia did not influence arterial lactate concentrations or pH during either submaximal or maximal exercise (Table 1), as is required according to the explanation of how hyperoxia improves performance according to the traditional anaerobiosis model. Third, in hyperoxia subjects terminated exercise when arterial pO_2 and sO_2 were much increased compared to exercise in normoxia

Thus these findings favour the alternate interpretation that hyperoxia improves exercise performance by altering afferent sensory feedback to a postulated central governor by increasing arterial O_2 content and hence the delivery of oxygen to oxygen-sensitive organs such as the heart, brain or respiratory muscles (Noakes et al, 2001). According to this model, exercise terminates specifically to ensure that homeostasis is maintained, that is before there is any evidence for homeostatic failure. That homeostasis is maintained under all conditions of normoxia and hyperoxia is clearly shown in these experiments and is underlined by the fact that the arterial pH and lactate concentrations are were similar throughout the trials and at fatigue, even for the hyperoxic trials in whcih the subjects attained a significantly higher workload. The similar concentration of lactate at the end of the trials might previously have been interpreted as a cause of fatigue however, Nielsen et al (2001) have recently shown that far from being an inhibitor of skeletal muscle

contractile function, hydrogen ions may actually "act to protect the function of skeletal muscle during high intensity exercise". In hyperoxia subjects terminated exercise even though their arterial pO_2 was increased, which indicates that reduced arterial pO_2 is unlikely to be the single cause of exercise termination. However, the finding that subjects terminated exercise at a similar V_Emax might suggest that afferent sensory feedback from the ventilatory muscles to a postulated central governor may be operative. Indeed there is evidence that V_Emax is usually similar regardless of the testing protocol or intervention (Mancini et al, 1997; Peper et al, 1982).

TABLE 1

Changes in arterial pO_2, pCO_2, pH, [La], sO_2 and O_2Hb during maximal exercise in a sealed pressure chamber with F_IO_2 of 21, 35 or 60% O_2.

		Rest	3 min	6 min	Fatigue
pO_2 (mmHg)	21%	$111 \pm 11^{b,c,d,f,g}$	$92 \pm 10^{a,f,g}$	$92 \pm 11^{a,e,g}$	$94 \pm 8^{a,f,g}$
	35%	$223 \pm 12^{d,e,g}$	$217 \pm 8^{e,g}$	$212 \pm 22^{e,g}$	$203 \pm 21^{a,e,g}$
	60%	$354 \pm 25^{b,c,d,e,f}$	$369 \pm 39^{a,e,f}$	$373 \pm 10^{a,e,f}$	$371 \pm 12^{a,e,f}$
PCO_2 (mmHg)	21%	36 ± 4	38 ± 6^{d}	36 ± 6	34 ± 5^{b}
	35%	35 ± 4^{b}	40 ± 3^{a}	37 ± 5	36 ± 4
	60%	$34 \pm 9^{b,c}$	40 ± 6^{a}	39 ± 6^{a}	38 ± 7
pH	21%	$7.42 \pm 0.02^{b,c,d}$	$7.35 \pm 0.03^{a,c,d}$	$7.30 \pm 0.05^{a,b,d}$	$7.27 \pm 0.03^{a,b,c}$
	35%	$7.40 \pm 0.05^{b,c,d}$	$7.31 \pm 0.05^{a,c,d}$	$7.26 \pm 0.06^{a,b,d}$	$7.23 \pm 0.06^{a,b,c}$
	60%	$7.42 \pm 0.04^{b,c,d}$	$7.33 \pm 0.03^{a,c,d}$	$7.28 \pm 0.03^{a,b,d}$	$7.26 \pm 0.04^{a,b,c}$

[La] (mmol.L^{-1})	21%	1.2 ± 0.3[b,c,d]	5.6 ± 2.3[a,c,d]	12.1 ± 3.6[a,b]	13.8 ± 3.2[a,b]
	35%	1.4 ± 0.5[b,c,d]	6.1 ± 3.7[a,c,d]	12.5 ± 3.6[a,b]	14.0 ± 3.1[a,b]
	60%	1.5 ± 0.4[b,c,d]	5.5 ± 2.3[a,c,d]	11.6 ± 5.3[a,b]	13.6 ± 5.1[a,b]
sO_2 (%)	21%	98.6 ± 0.4[b,c,d,f,g]	97.3 ± 1.3[a,c,d,f,g]	96.7 ± 1.4[a,b,f,g]	96.4 ± 1.5[a,b,f,g]
	35%	99.3 ± 0.2[e]	99.2 ± 0.2[e]	99.0 ± 0.2[e]	98.8 ± 0.1[e]
	60%	99.7 ± 0.1[e]	99.5 ± 0.2[e]	99.5 ± 0.2[e]	99.4 ± 0.2[e]
O_2Hb (%)	21%	95.6 ± 0.3[b,c,d,f,g]	94.5 ± 1.2[a,c,d,f,g]	93.9 ± 1.3[a,b,f,g]	93.7 ± 1.4[a,b,f,g]
	35%	96.5 ± 0.2[e]	96.4 ± 0.2[e]	96.3 ± 0.2[e]	96.2 ± 0.2[e]
	60%	96.6 ± 0.3[e]	96.6 ± 0.2[e]	96.6 ± 0.2[e]	96.6 ± 0.2[e]

[a] Significantly different from Rest ($p < 0.05$)
[b] Significantly different from 3 min ($p < 0.05$)
[c] Significantly different from 6 min ($p < 0.05$)
[d] Significantly different from Fatigue ($p < 0.05$)
[e] Significantly different from 21% ($p < 0.05$)
[f] Significantly different from 35% ($p < 0.05$)
[g] Significantly different from 60% ($p < 0.05$)

LEGEND TO FIGURES

Figure 1 Mean maximum values of VO_2, V_E, and power output attained during maximal exercise in a sealed pressure chamber with F_IO_2 of either 21, 35 or 60% O_2.

* 21% is significantly different from 35% and 60% O_2 ($p < 0.05$)

Figure 2 Comparison of individual peak power outputs for each subject during maximal exercise with F_IO_2 of 21 (■), 35 (▩) and 60 (□)% O_2.

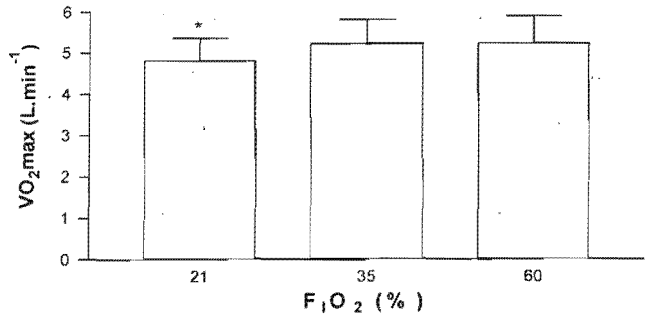
Figure 3 Submaximal VO_2, VCO_2, V_E and RER for the initial 360 s of progressive maximal exercise performed according to a ramp protocol with F_IO_2 of 21 (•), 35 (x) and 60 (O)% O_2.

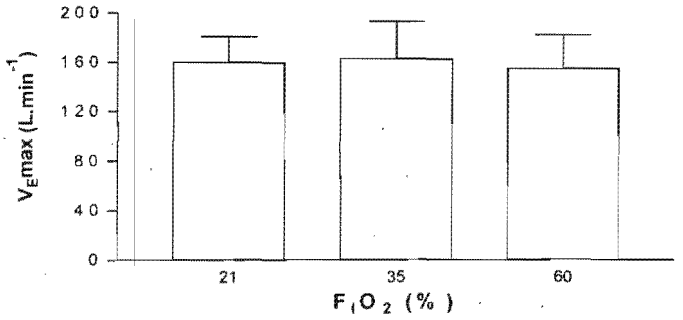
* 21% is significantly different from 35% and 60% O_2 ($p < 0.05$)

λ 21% is significantly different from 35% ($p < 0.05$)

Figure 4 VO_2, VCO_2, V_E and RER for the final 330 s of maximal exercise performed according to a ramp protocol with F_IO_2 of 21 (•), 35 (x) and 60 (O)% O_2.

FIGURE 1





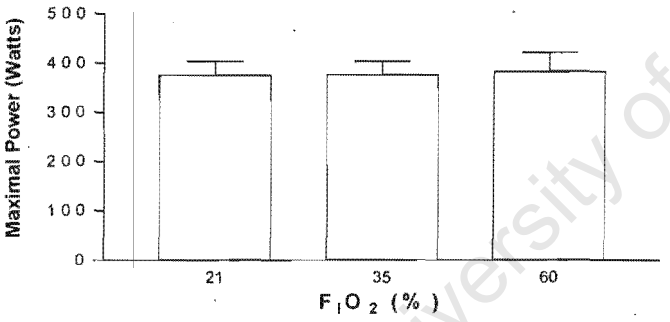


FIGURE 2

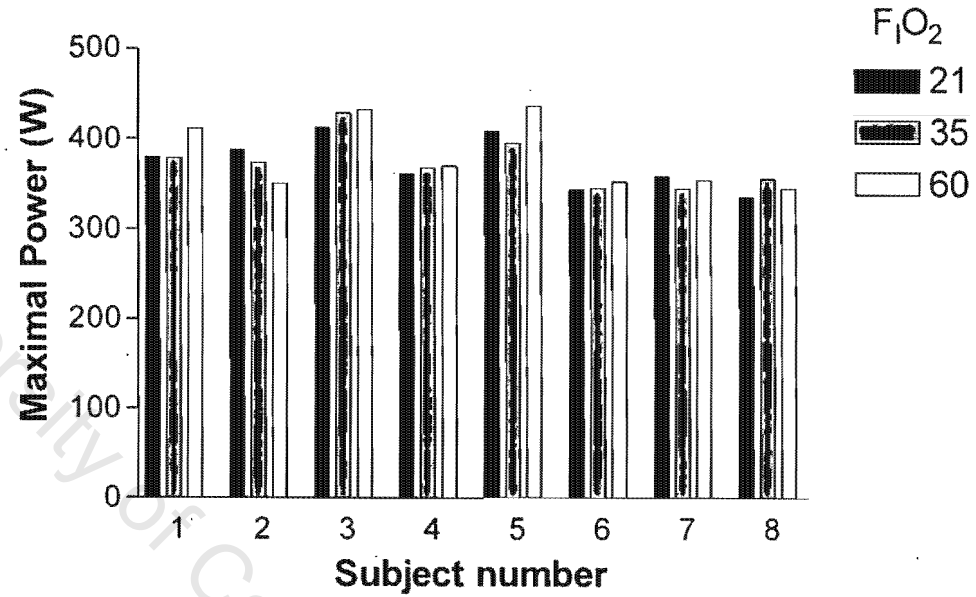


FIGURE 3

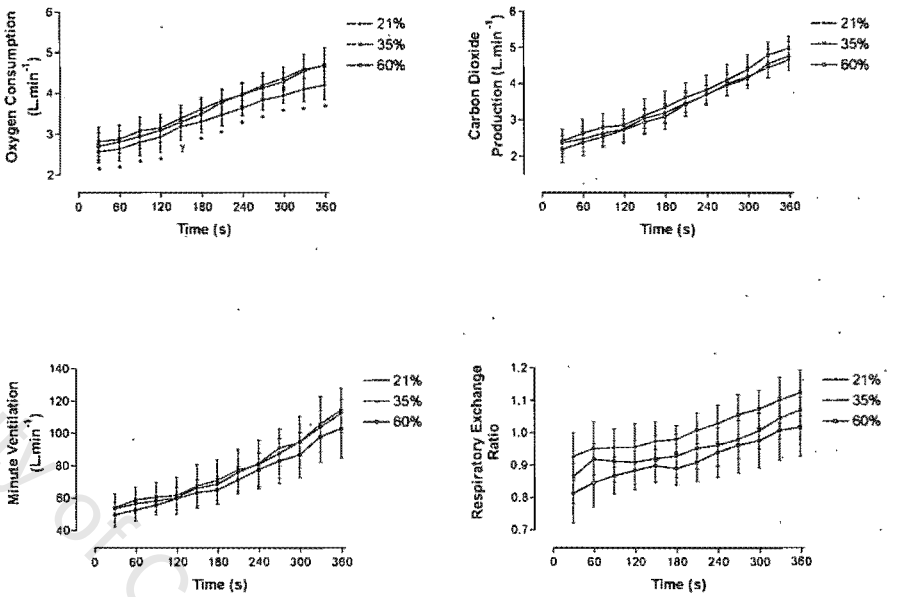
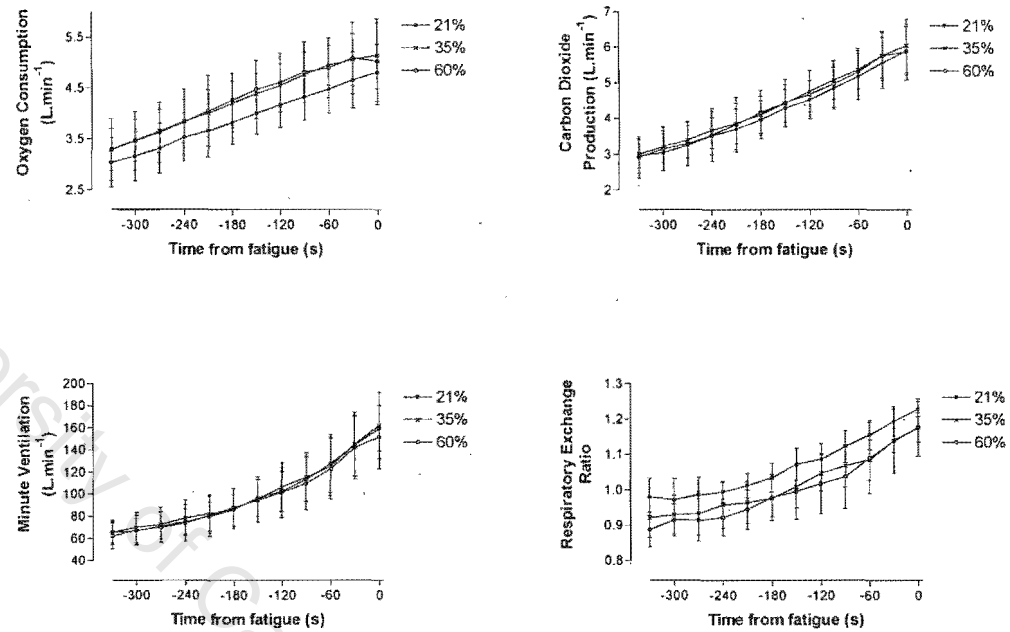


FIGURE 4



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V) RELIABILITY AND INTER-CHANGEABILITY OF TWO POPULAR AUTOMATED METABOLIC GAS ANALYSIS SYSTEMS

Introduction

Scientists have long been interested in quantifying human energy expenditure at rest and during physical activity. But it was only in 1911 that Douglas (1911) developed the 'Douglas bag' technique that is today considered the gold standard (Basset et al, 2001) in measuring gas exchange in exercising individuals. This method involves the collection of all the expired air over a measured period into a large bag. A small volume is removed for analysis of expired gas fractions of oxygen and carbon dioxide by a gas analyser while the remaining gas is evacuated through a flow meter for the determination of ventilatory volume. Although this refined technique is simple and accurate, it remains time consuming and labour intensive.

The development over the last 30 years of reliable automated metabolic gas analysers has resulted in a large number of laboratories choosing these complex automated gas analysis systems over the traditional Douglas bag method for the measurement of oxygen consumption (VO_2) and carbon dioxide (CO_2) production. The improvement in technology since the early, automated analysers has provided for highly valid and reliable measurements of VO_2 in the modern computerised systems. However, despite these developments large variability in the measurement of metabolic parameters exists between different brands of automated systems. This variability would seem to undermine the results of studies that have compared the metabolic variables recorded from different centres.

The purpose of this study was to test the reliability and interchangeability of the Schiller CS-200 against the Vmax Series 229, two widely used automated metabolic analysers, during submaximal workloads between 200 and 325 W.

Materials and methods

Gas analysers

Schiller CS-200

The CS-200 Ergo-Spiro, Schiller (Switzerland) measures flow rate through a diaphragm spiroceptor, with a measurement range of 0 – 16 $L.s^{-1}$. A flexible screen is used to enhance the laminar flow of the gas through the pneumotachometer. Gas flow is integrated over time to calculate expired gas volume (range 0 – 300L):

$$V_E = \frac{\sum_{1}^{\text{Respiration}} \left(\int_{\text{End Inspiration}}^{\text{End Expiration}} \text{Flow}(t) \cdot dt \right)}{\text{Respiration}}$$

Equation 1

For the analysis of O_2 and CO_2 fractions in the expired air the CS-200 uses a electrochemical cell oxygen analyser (range 0 – 100%) and ultrasound density carbon dioxide analyser (range 0 – 17.5%), respectively. The paramagnetic properties of oxygen in a gas sample cause the rotation of a nitrogen-filled glass dumbbell when suspended in a magnetic field. Quantifying the amount of rotation of the dumbbell or of the current required to cancel the rotation provides a measure directly proportional to the oxygen concentration in the sample. VO_2 and VCO_2 are then calculated from digital integration of the flow and difference between the respective inspired and expired gas fractions:

$$VO_2 = \frac{\sum_{1}^{\text{Respiration}} \left(\int_{\text{End Inspiration}}^{\text{End Expiration}} \text{Flow}(t) \cdot FO_2 \cdot dt \right)}{\text{Respiration}}$$

Equation 2

and

$$VCO_2 = \frac{\sum_{1}^{\text{Respiration}} \left(\int_{\text{End Inspiration}}^{\text{End Expiration}} \text{Flow}(t) \cdot FCO_2 \cdot dt \right)}{\text{Respiration}}$$

Equation 3

where:

Flow is the rate of gas flow, F is the difference between inspired and expired gas fractions and t is time

Vmax Series 229

The Vmax 229 Series, Sensor Medics (California) utilises a hotwire anemometer, or mass flow sensor, for the determination of gas volume. As gas passes over a thin heated wire the temperature of the wire drops in proportion to the mass and flow of the gas, thus more current is supplied by the feedback circuit to maintain the wire at a preset temperature. The supplied current is proportional to the gas flow and is integrated over time to provide gas volumes. In the Vmax Series 229 there is a 2-wire sensor with one wire acting as a reference. Analysis of the fraction of O_2 in expired air was via a chemical paramagnetic fuel cell oxygen analyser where the paramagnetic properties of oxygen in a gas sample cause the rotation of a nitrogen-filled glass dumbbell when suspended in a magnetic field. Quantifying the amount of rotation of the dumbbell or of the current required to cancel the rotation provides a measure directly proportional to the oxygen concentration in the sample. Fractional CO_2 is determined from non-dispersive infrared, in which dual beams of infrared radiation are passed through a reference cell and parallel sample cell containing the test gas at a

constant flow. This measurement relies on the fact that CO_2 absorbs the infrared beam. VO_2 and VCO_2 are calculated from the formulas:

$$VO_2 = V_E \times (F_IO_2 \cdot \frac{1 - F_EO_2 - F_ECO_2}{1 - F_IO_2 - F_ICO_2} - F_EO_2)$$

Equation 3

and

$$VCO_2 = V_E \cdot (F_ICO_2 - F_ECO_2)$$

Equation 4

where:

F_I is inspired gas fraction and F_E is expired gas fraction

Test protocol

Eight well-trained subjects cycled at five discrete workloads of increasing intensity on two occasions separated by 7 days. The exercise was performed on an electrically braked Lode cycle ergometer (Excalibur, Netherlands) at a self-selected cadence at workloads of 200, 250, 275, 300 and 325 W. A recovery period of 3 min was allowed between intervals during which the subjects recovered by cycling at 75 W. The subjects cycled for 7 min at each workload with gas collection occurring from 3 to 6 min. Metabolic variables were measured using open circuit spirometry with either the CS-200 or the Vmax 229 Series.

Ratings of perceived exertion

Printed instructions were provided to familiarise subjects with the scale prior to their first trial. No prompting was given by the researcher in translating

their feeling into numerical ratings on the RPE scale. The Borg category-ratio exertion scale was used to quantify exertion localised specifically to the effort of breathing. The category-ratio scale was selected to measure localised exertion because the growth of this scale more closely parallels the exponential increase in ventilation during progressive exercise to exhaustion(Hassmen, 1990; Noble, 1982; Noble et al, 1983).

Statistical analysis

Oxygen consumption, carbon dioxide production, minute ventilation and respiratory exchange ratio were averaged over 10 s and the median 13 averages for each workload were used for analyses. Differences between and within maximum and submaximum data were identified by a Student's t-test and repeated measures Analysis of Variance, respectively. Once main effects were identified individual differences between the means were located using a Tukey's *post hoc* procedure. Pearsons's correlation co-efficient (r) were also calculated for VO_2, VCO_2, V_E and RER in order to determine the degree of correlation between measurements made by the different testing methods. Further analysis of validity of these measures was accomplished by applying the techniques suggested by Bland and Altman (1986). For this analysis, the mean differences (bias) and standard deviation (SD) of the differences of the values for the two methods were calculated. The data were presented graphically comparing the difference between the methods versus their average value. The mean difference plus and minus two standard deviations was indicated on the graph. In this way bias and precision could be calculated. Significance was accepted at $p < 0.05$. All statistical analyses were performed using Statistica® 6.0. Data are expressed as mean ± standard deviation (S.D.).

Results

Oxygen consumption

The oxygen consumption (VO_2) was not different between the Schiller and Vmax at any workload (Table 1). In both trials VO_2 increased significantly over successive workloads (Figure 1) ($p < 0.05$). A Bland-Altman plot reveals a mean difference of 0.37 $L.min^{-1}$ with 95% confidence interval 0.34 to 0.43 $L.min^{-1}$ and limits of agreement -0.53 and 1.30 $L.min^{-1}$ (Figure 2) The VO_2 results from the analysers were significantly correlated ($r = 0.78$) ($p < 0.05$) (Figure 3). The coefficient of variation was 2.4% for the Schiller and 3.1% for the Vmax.

Carbon dioxide production

The mean VCO_2 was significantly lower in the Schiller trial at 250, 275, 300 and 325 W ($p < 0.05$) (Table 1). The VCO_2 increased as a function of workload during both trials (Figure 1) ($p < 0.05$). The mean difference between the methods is 0.60 $L.min^{-1}$ and the limits of agreement lie at –0.39 to 1.58 $L.min^{-1}$ (Figure 2). The difference in the VCO_2 analysis between the analysers displays a 95% confidence interval 0.55 – 0.64 $L.min^{-1}$. The correlation co-efficient for VCO_2 between the two methods was significant at $r = 0.80$ ($p < 0.05$) (Figure 3). The coefficient of variation for the Schiller and Vmax was 2.7 and 3.7%, respectively.

Minute ventilation

There was no difference between minute ventilation (V_E) determined by the Schiller and Vmax at any workload (Table 1). In both trials V_E increased significantly over successive workloads (Figure 1) ($p < 0.05$). The mean difference between the trials was 4.0 $L.min^{-1}$ in an agreement range of –22.3 to

30.3 L.min^{-1} (Figure 2). The 95% confidence interval for the difference between trials was 2.8 to 5.2 L.min^{-1}. V_E displayed a significant correlation ($r = 0.82$) ($p < 0.05$) between analysers (Figure 3). The Schiller had a coefficient of variation of 3.9% while the Vmax had a CV of 5.4%.

Respiratory exchange ratio

The respiratory exchange ratio (RER) was similar between the Schiller and Vmax at all workloads (Table 1) and increased as a function of workload (Figure 1) ($p < 0.05$). The mean difference between trials was 0.05 with limits of agreement -0.03 to 0.13 (Figure 2) and a 95% confidence interval of 0.05 to 0.06. There was a significant correlation in RER between the trials ($r = 0.72$) ($p < 0.05$) (Figure 3 – left column). The predicted RER (± 0.04) is plotted against the actual RER calculated by the Schiller in Figure 3 (right column). The variation in RER for the Schiller and Vmax was 1.7 and 2.0%, respectively.

Perceived effort

The effort of breathing was not different between the trials at any workload (Table 1). The effort involved in breathing increased as a function of workload in both trials.

Discussion

Results indicate that the Schiller CS-200 and the Vmax Series 229 automated metabolic carts are reliable measures of expired metabolic gas and are highly correlated. However care should be taken in directly comparing studies that have used the two different systems due to the relatively poor agreement of results measured by the two systems.

The correlations between the methods for measuring the metabolic parameters were significant for all the metabolic parameters (Figure 3) indicating that the measurements by the Schiller CS-200 and the Vmax Series 229 are highly related. Although the correlations co-efficient suggest a good relationship between the two systems it has been convincingly argued that a high correlation does not necessarily mean that the two systems are in agreement (Altman et al, 1983; Atkinson, 1995; Bland et al, 1986). These authors suggest that in order to assess whether different methods agree it is more suitable to plot the difference between methods against the mean of the two methods (Figure 2).

The Bland-Altman plot of the data shows that the mean difference in VO_2 between the Schiller CS-200 and the Vmax Series 229 is 0.37 $L.min^{-1}$ and the 95% confidence intervals indicate that the Schiller CS-200 tends to give a lower reading by between 0.34 and 0.43 $L.min^{-1}$. However, the amount of disagreement ranges from –0.53 to 1.30 $L.min^{-1}$, which may be too large for clinical purposes. Similarly although the mean difference between V_E (4.0 $L.min^{-1}$) lies within a 95% confidence interval of 2.8 to 5.2 $L.min^{-1}$ the limits of agreement are relatively large (-22.3 to 30.3 $L.min^{-1}$) signifying that there can be considerable discrepancies between the two methods that may not be acceptable in clinical conditions. Although the VCO_2 during the submaximal workloads above 200 W differs between the two methods (Table 1 and Figure

1), the Bland–Altman plot suggests that the two methods can still be used interchangeably in scientific exercise testing although once again care must be taken to identify the levels of agreement which are acceptable within the experiment. Moreover the differences in the VCO_2 do not result in a difference in the RER (Table 1 and Figure 1). Therefore substrate utilisation during steady state exercise can be measured confidently with either system.

Both systems displayed low variability in the measurement of metabolic parameters during the submaximal exercise indicating good reliability of the two systems. However, the range of variability in the Schiller CS-200 (2.4 – 3.9%) was consistently lower than the Vmax Series 229 (3.1 – 5.4%).

In conclusion, at workloads between 200 and 325 W the results obtained from the Schiller CS-200 and Vmax Series 229 exhibit a close relationship but the limits of agreement are wide, which reflects a variation of the differences. The limits of agreement illustrate that there can be considerable discrepancies between the two systems and that the Schiller CS-200 and Vmax Series 229 automated gas analysis cannot be used interchangeably. However, the Schiller CS-200 and the Vmax Series 229 still provide reliable measures of VO_2, VCO_2, V_E and RER during submaximal exercise.

TABLE 1

Comparison of VO_2, VCO_2, V_E, RER and RPE determined at different workloads by the Schiller CS-200 and the Vmax Series 229 metabolic carts.

	Watts	Schiller	Vmax
VO_2 ($L.min^{-1}$)	200	3.2 ± 0.3	3.4 ± 0.3
	250	3.8 ± 0.3	4.1 ± 0.5
	275	4.1 ± 0.3	4.5 ± 0.4
	300	4.3 ± 0.2	4.7 ± 0.4
	325	4.6 ± 0.2	5.3 ± 0.5
VCO_2 ($L.min^{-1}$)	200	2.9 ± 0.2	3.2 ± 0.3
	250	3.5 ± 0.3*	4.1 ± 0.4
	275	3.9 ± 0.4*	4.6 ± 0.5
	300	4.1 ± 0.2*	4.8 ± 0.3
	325	4.5 ± 0.3*	5.4 ± 0.5
VE ($L.min^{-1}$)	200	67 ± 6	68 ± 67
	250	83 ± 12	88 ± 12
	275	97 ± 17	103 ± 19
	300	103 ± 15	105 ± 10
	325	113 ± 18	122 ± 15
RER	200	0.90 ± 0.03	0.95 ± 0.03
	250	0.94 ± 0.04	0.99 ± 0.04
	275	0.96 ± 0.04	1.01 ± 0.06
	300	0.97 ± 0.05	1.02 ± 0.05
	325	0.98 ± 0.04	1.03 ± 0.04
RPE	200	2.6 ± 0.7	1.9 ± 0.8
	250	3.2 ± 1.1	2.8 ± 0.6
	275	4.3 ± 1.6	3.8 ± 1.1
	300	4.6 ± 1.1	4.3 ± 1.2
	325	4.9 ± 0.2	4.8 ± 0.5

* Significant difference between Schiller CS-200 and Vmax Series 229 ($p < 0.05$)

LEGEND TO FIGURES

Figure 1 Comparison between individual VO_2, VCO_2, V_E and RER measured with Schiller CS-200 (—) and Vmax Series 229 (···) at 200, 250, 275, 300 and 325 W.

Figure 2 Bland-Altman plot depicting calculated bias and individual differences (mean ± 2SD) for VO_2, VCO_2, V_E and RER.

Figure 3 Individual values for VO_2, VCO_2, V_E and RER from Schiller CS-200 plotted against the individual values from Vmax Series 229, with the line of equality.

FIGURE 1

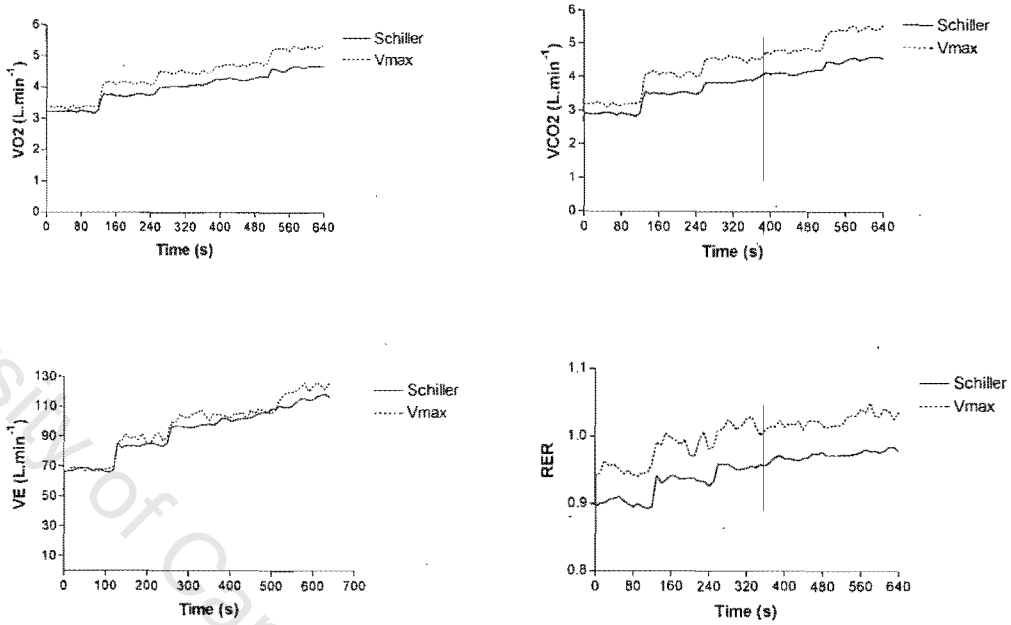
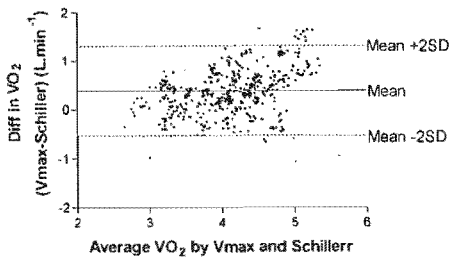
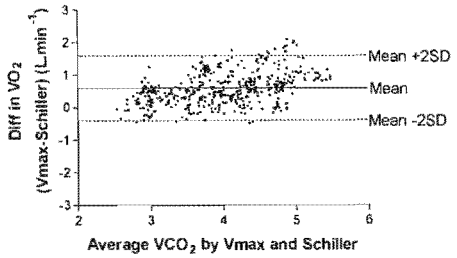
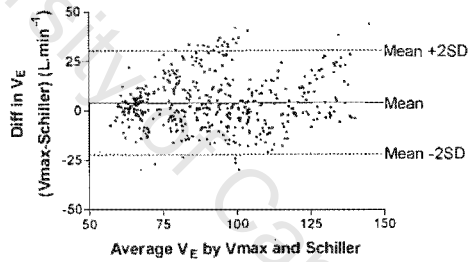


FIGURE 2







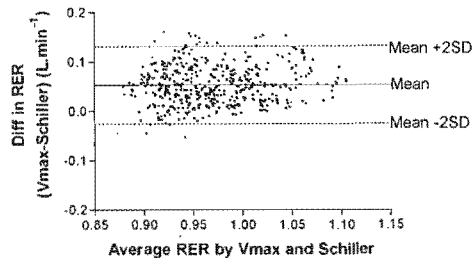
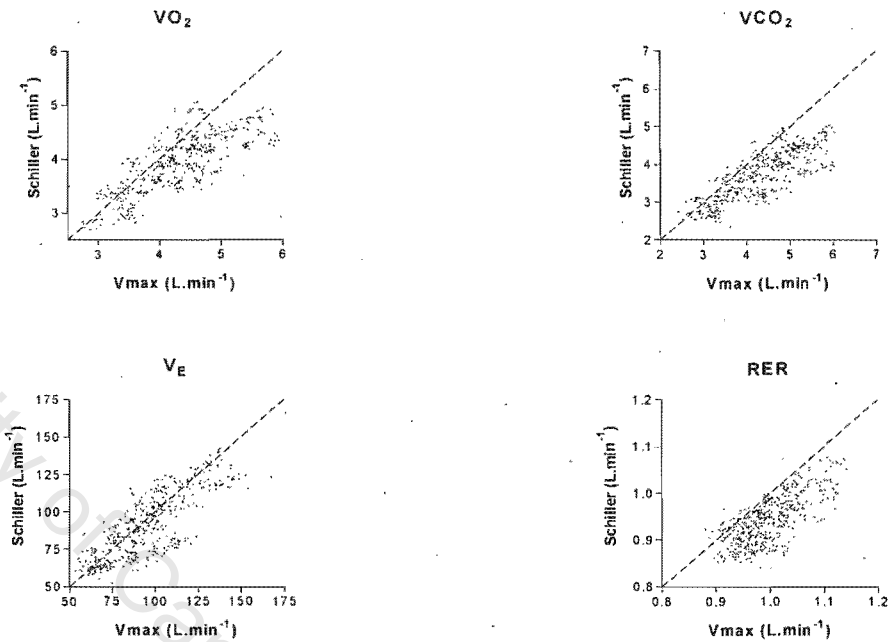


FIGURE 3



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VI) THE WORK OF BREATHING DOES NOT LIMIT THE MAXIMAL EXERCISE PERFORMANCE OF HUMANS AT SEA-LEVEL

The factors that cause the termination of progressive maximum exercise – the "exercise-stoppers" (Gandevia et al, 2000) – are poorly understood. The most popular explanation holds that exercise terminates when skeletal muscle anaerobiosis develops causing an uncompensated lactic acidosis that inhibits skeletal muscle contractile function (Basset et al, 2000).

However, four significant arguments contest this explanation. First, the decision to terminate exercise is clearly a conscious choice, indicating that the central nervous system must play at least some part in the termination of exercise (Gandevia, 2001). Second this peripheral model of exercise regulation is clearly unable to explain what limits maximum exercise at extreme altitude since blood lactate concentrations are no higher at exercise termination than they are under resting conditions at sea level (Green et al, 1989). Furthermore, the peak cardiac output is reduced at altitude (Sutton et al, 1992) even though myocardial function is unaffected by the hypoxia of altitude (Noakes et al, 2001). If skeletal muscle anaerobiosis limits maximal exercise at altitude one would expect that the same maximum cardiac output would be achieved both at altitude and sea level. Rather, maximum exercise at altitude terminates at lower levels of motor unit recruitment than are achieved at sea level (Kayser et al, 1994) indicating that at altitude "the central nervous system may play a primary role in limiting exhaustive exercise and the maximum accumulation of lactate in blood, as originally proposed in 1984 by Bigland-Ritchie and Woods (1984).

Indeed, the third finding that is incompatible with this peripheral model of exercise regulation is that both maximal but especially prolonged submaximal exercise (St Clair Gibson et al, 2001) terminates without complete recruitment of all the available motor units in the active limbs. It is difficult to understand

how metabolite-induced inhibition of skeletal muscle contractile function can also regulate the function of a large number of quiescent motor units that have yet to be recruited at exhaustion. Rather, an exclusively peripheral model of exercise regulation predicts that exercise termination can only occur when all the available motor units in the exercising muscles are recruited and their function is then inhibited by the appropriate change in intracellular metabolite concentrations.

The fourth finding challenging the traditional explanations is the recent finding apparently showing that lactic acid, far from being an inhibitor of skeletal muscle contractile function, may actually "act to protect the function of skeletal muscle during high intensity exercise" (Nielsen et al, 2001). Others have also provided recent evidence that lactate is not an inhibitor of skeletal muscle contractile function (Posterino et al, 2001). But if lactic acid is not the peripheral inhibitor of muscle function as originally proposed by A.V. Hill and colleagues in the 1920's (1923; 1924a; 1924b; 1925), then the central pillar of this peripheral model of exercise regulation (Basset et al, 2000) has been removed and an alternate explanation would seem to be required (Noakes, 1997; Noakes, 2000).

In a previous study (Nobbs et al, 2003) we showed that exercise in hyperoxia (F_IO_2 of 35 and 60%) performed in a pressure sealed chamber that allows the inhalation of the gas mixtures directly from the surrounding environment, significantly increased arterial blood oxygen content throughout progressive maximum exercise to exhaustion. Maximum oxygen consumption (VO_2max) was also significantly increased although the effect on maximal work rate was more equivocal. Thus despite significantly increased arterial oxygen content and a higher rate of oxygen consumption, the work rate at which exercise terminated changed relatively little (~10 W or 2%). More importantly,

exercise terminated even though arterial oxygen concentrations were significantly elevated (pO_2 of 354 ± 25 mmHg at F_IO_2 of 65%) and were not reduced at exhaustion. Thus neither an absolute arterial pO_2 nor its rate of fall caused the termination of exercise in that study.

This latter finding would also seem to discount that component of the alternate, central governor, theory of exercise regulation which predicts that afferent sensory information from oxygen-sensitive organs like the heart, brain or respiratory muscles, limits the recruitment of additional motor units by central neural mechanisms, when the oxygen delivery to those organs is compromised (Noakes et al, 2001)

Surprisingly, ventilation was unaltered during either submaximal or maximal exercise in F_IO_2 of either 35 or 60% compared to exercise in normoxia. This raised the alternate possibility that sensory feedback from the respiratory muscles might provide the afferent information to the postulated "central governor" (Noakes et al, 2001) that purportedly regulates exercise performance according to that model. It is known, for example, that the J reflex in animals that is stimulated by the activation of pulmonary C fibres inhibits muscle recruitment (Gandevia et al, 2000). However, the presence of this reflex in humans appears unlikely (Gandevia et al, 2000).

On the other hand, it is known that increasing inspiratory airflow resistance reduces maximum exercise performance (Dressendorfer et al, 1977) indicating a potential role for afferent sensory feedback from the respiratory muscles in determining maximum exercise performance also in humans.

Accordingly the hypothesis to be tested in this study is that, if receptors in the respiratory muscle sensing respiratory muscle work play a role in the termination of maximal exercise in humans, then exercise performance should

be enhanced in an environment in which airflow resistance and hence the work of breathing is reduced. Helium is one such agent that reduces the resistance to airflow in the respiratory tree by ensuring laminar flow at high flow rates (Glauser et al, 1969; Otis et al, 1949).

Accordingly, for this study we used the same methods as in our previous study (Nobbs et al, 2003) to compare progressive maximum exercise performance in conditions of normoxia and hyperoxia and in hyperoxia in which the inspired air was also helium-enriched (heliox). Our aim was to determine the physiological consequences of reducing the resistance to airflow in the respiratory tree under conditions of maximal exercise when arterial pO_2 remained elevated during exercise. If sensory afferent feedback from the respiratory muscles, sensing the work of breathing, limits the peak work rate by setting an absolute achievable rate of respiratory work, hence acting as the exercise "stopper" (Gandevia et al, 2000), then maximum exercise performance in a helium-enriched environment should be increased in direct proportion to the extent to which helium unloads the work of the respiratory muscles during exercise.

Furthermore since subjects inhaled the different gas mixtures directly from the environment of the pressure-sealed chamber, and not from a length of respiratory tubing attached to gas mixing bags, we studied exclusively the direct effect of unloading respiratory muscle work rather than any effects on this physiological resistance, combined with any artificial resistance imposed by the experimental methods used to deliver the altered gas mixtures.

Methods

Subjects

Eight highly trained cyclists were recruited for this study, which was approved by the Research and Ethics Committee of the Faculty of Health Sciences of the University of Cape Town. The nature of the study including the risks associated with exercising in oxygen and helium enriched conditions was clearly explained to the subjects after which informed consent was obtained from each subject prior to the initiation of testing. The mean age, height and weight of the subjects were 20.1 ± 1.2 years, 184.4 ± 5.6 cm and 69.6 ± 5.1 kg, respectively.

Experimental protocol

The protocols used are similar to those used in our previous study (Nobbs et al, 2003). Each subject was required to perform an incremental ramp cycle test to exhaustion on a Lode cycle ergometer (Excalibur, Netherlands) on three separate occasions, while breathing room air, a hyperoxic mixture (F_IO_2 of 35% and the balance nitrogen) and a heliox mixture (F_IO_2 of 35% and the balance helium). Consecutive tests were separated by at least two days and were not more than seven days apart and the testing order was randomised and single-blinded. The cycle ergometer ramp protocol consisted of a 2 min warm-up ride at 150W, thereafter the workload of the ramp protocol increased by 0.5W.sec^{-1} to volitional exhaustion.

All tests were performed in a pressure sealed chamber. Once the subjects and researcher had entered the chamber, the chamber was filled with the required gas mixture depending on the trial to be performed. Once the door had been sealed no talking was permitted in the chamber since talking would identify

the presence of a helium-enriched environment. For the heliox trials the chamber was completely flushed through twice (36 000 L) with the helium/oxygen mixture after the door was sealed. The chamber was not pressurised for any test and the F_IO_2 was continuously monitored. Typically, the percent F_IO_2 in the hyperoxic trials did not drop more than 1 - 2% throughout the duration of the trial.

Prior to each test, subjects sat quietly for 10 minutes in the chamber while breathing the imposed gas mixture to ensure adequate equilibration of the inhaled gas mixtures throughout the body and also complete mixing of the new gas mixture throughout the chamber. During the trial, a fan maintained continual air movement within the chamber to prevent any gas layering that might occur with the low-density mixture. Continuous monitoring of the chamber F_IO_2 at the height of the cyclist's head confirmed that the different gasses were homogenously mixed throughout the trials especially those involving the helium mixture. The test was followed by a recovery period during which the chamber was flushed through twice with room air to preclude the subjects identifying the nature of the gas mixture that had been present during their trials.

Pressure-sealed Chamber

The subjects cycled inside a Multi-place Class "A" 18 000 L hyperbaric chamber of length 3.5 m and diameter 2.5 m built to Lloyd's and ASME 1 PVHO specifications. There were internal CO_2 scrubbers and O_2, temperature and humidity were continuously monitored. An oxygen sensor placed at head height for the subjects on the ergometer continuously monitored the F_IO_2 in the ambient air. When the F_IO_2 dropped 2% below the required percentage, the relevant gas mixture was fed into the chamber until the requisite F_IO_2 was achieved.

Expired respiratory gas analyses

For the measurement of oxygen consumption (VO_2), carbon dioxide production (VCO_2) and minute ventilation (V_E) during the tests, subjects wore a mask covering the nose and mouth. The expired air passed through an on-line breath-by-breath gas analyser and pneumotach (Cardiovit CS-200 Ergo-Spiro, Schiller, Switzerland). Before each test the pneumotach was calibrated with a 2L syringe and the gas analyser by a calibration gas composed of 15.6% O_2: 4.1% CO_2. Oxygen consumption and CO_2 production were calculated according to the following equations:

$$VO_2 = \frac{\sum_{1.}^{\text{Respiration}} \left(\int_{\text{End Inspiration}}^{\text{End Expiration}} \text{Flow}(t) \cdot FO_2 \cdot dt \right)}{\text{Respiration}}$$

and

$$VCO_2 = \frac{\sum_{1.}^{\text{Respiration}} \left(\int_{\text{End Inspiration}}^{\text{End Expiration}} -\text{Flow}(t) \cdot FCO_2 \cdot dt \right)}{\text{Respiration}}$$

where: Respiration is the volume of gas in the sample

Flow is the rate of gas flow through the pneumotachograph

FO_2 is the fraction of oxygen in the expired air

FCO_2 is the fraction of CO_2 in the expired air

t is the time over which the expired gas was sampled

All data were averaged over 30 seconds. Maximal oxygen consumption (VO_2max) was defined as the highest VO_2 measured during the test. Minute ventilation was determined from the pneumotach.

Integrated electromyography (iEMG)

Maximal voluntary contractions

Before each trial an MVC was performed on a locally designed system for the measurement of neuromuscular and musculotendinous stiffness (Zest Manufacturing PTY (LTD) and U.C.T., Cape Town, South Africa). In this system, the subject sits in the position to perform the leg press exercise with the knee at a 95° angle when full extension is referenced as 0°. This position was chosen to create a functional measure of iEMG using muscle groups in a position similar to that used during cycling. The vastus lateralis muscle was used as a measure of neural activation during cycling. Two surface EMG electrodes (blue sensor SP-00-S, Medicotest A/S, Rugmarken, Denmark) were attached as a pair over the muscle belly with an inter-electrode distance of ~2cm (Strojnik et al, 1998). A third neutral reference electrode was placed on the tibial tuberosity. The site for electrode placement was determined as the centre of the muscle belly when contracting isometrically, and the electrodes were attached running parallel to the muscle fibres (Kay et al, 2000). Before the electrodes were attached, the skin surface was prepared. Hair was shaved off with a razor and the skin was scraped with sandpaper to remove the outer layer of epidermal skin cells. The skin surface was then swabbed clean with an alcohol swab that removed any oils or dirt. Once the alcohol had evaporated, the electrodes were placed on the skin (Kay et al, 2000).

All raw EMG data were sampled at 2000Hz using MyoResearch 2.02 (Noraxon USA Inc, Scottsdale, Arizona, USA) software and a telemetric EMG system (Noraxon USA, Inc., Scottsdale, Arizona, U.S.A.). EMG data were then full-wave rectified, and smoothed root mean square. Typical noise and artefact from power lines was removed using a 60 Hz notch filter. A Butterworth six-pole filter was applied and finally the data were subjected to a bandpass filter for 10 – 200 Hz and integrated for further analysis. Electromechanical delay was treated as a systematic error, as it was assumed that this was either negligible or constant (Gollhofer et al, 1991).

Each subject was given three sub-maximal warm-up trials in which they were instructed to push at their perceived 50, 70 and 90% of maximum, respectively, against the fixed foot plates. Three maximal trials per subject followed the warm-up. The subjects were instructed to push as fast and as hard as possible, maintaining the contraction for 3 seconds against the isometric resistance. The researchers gave vocal encouragement to ensure that the subjects gave maximal effort during the MVC. The integrated EMG obtained from the three trials was recorded and used to normalize the EMG values of the subsequent incremental ramp cycle ergometer test.

Ratings of perceived exertion

Levels of exertion were quantified on two different scales, the Borg 15-point RPE scale (RPE_{15}) and the Borg category-ratio scale (RPE_{10}). Printed instructions were provided to familiarise subjects with each scale prior to their first incremental ramp test. Subjects were asked to provide an appropriate single score on the 15-point scale that was the best representation of their overall level of exertion. No assistance was given by the researcher in translating their feeling into numerical ratings on the RPE scale. The Borg category-ratio exertion scale was used to quantify exertion localised specifically

to the effort of breathing. The category-ratio scale was selected to measure localised exertion because the growth of this scale more closely parallels the exponential increase in the ventilation during progressive exercise to exhaustion (Hassmen, 1990; Noble, 1982; Noble et al, 1983). Due to the mandatory silence maintained whilst they were in the chamber subjects were instructed to point at the appropriate rating on the scale held before them by the researcher in the chamber. To avoid misunderstanding they were not allowed to choose fractions of the scales or ratings below and above the limits of the scale.

Heart rate

Heart rate (HR) was recorded every 10 seconds using a Polar Accurex Plus heart rate monitor (Polar Electro, Kempele, Finland). The data were downloaded via an interface into hrm files after completion of the trial. Maximum HR during each test was taken as the highest HR recorded at any stage during the test.

Blood Sampling

A 20G Jelco™ cannula was inserted into a forearm vein in each subject before he entered the chamber. The first (resting) blood sample was drawn after the subject had rested in the chamber for 10 minutes to ensure complete equilibration of the new inspired F_IO_2. Thereafter blood was sampled every three minutes during the trial. During each sampling, 2 ml of blood was drawn into a vacutainer tube containing potassium oxalate and sodium fluoride for the measurement of plasma lactate concentrations.

Blood Analyses

Lactate

Blood samples for lactate analysis were stored on ice until centrifuged at 3000 x g for 10 min at 4°C and the plasma stored at -20°C. Plasma lactate concentrations were determined by spectrophotometric (Beckman Spectrophotometer – M35) enzymatic assays using a lactate kit (Lactate PAP, bioMérieux Kit, Marcey l'Etoile, France).

Statistical analyses

Data for submaximum VO_2, VCO_2, V_E and power output were averaged over 30 s from 0 to 330 s to avoid the confounding effect of subject dropout. For the comparison of VO_2, VCO_2 and V_E approaching fatigue, data was averaged retrospectively over 30 s from the point of fatigue. For maximum and submaximum data, a repeated measures Analysis of Variance was used to assess differences between and within the trials. Once main effects were identified individual differences between the means were located using a Scheffe *post hoc* procedure. Significance was accepted at $p < 0.05$. All data are expressed as mean ± standard deviation (S.D.).

Results

Maximum values of VO_2, VCO_2, V_E, RER and power output

Peak power output increased significantly ($p < 0.05$) in both the hyperoxic (451 ± 58 W) and heliox (453 ± 56 W) trials compared to exercise in F_IO_2 of 21% (429 ± 59 W) (Figure 1). However, peak power output was the same in the hyperoxia and heliox conditions. The VO_2max was not significantly different between trials (normoxia = 4.9 ± 0.7 L.min^{-1}; hyperoxia = 5.0 ± 0.6 L.min^{-1}; heliox = 4.9 ± 0.7 L.min^{-1}) (Figure 1). Maximal minute ventilation was also similar for all conditions (normoxia = 155 ± 24 L.min^{-1}; hyperoxia = 157 ± 24 L.min^{-1}; heliox = 163 ± 22 L.min^{-1}) (Figure 1). Due to the thermal properties of helium, the non-dispersive infrared CO_2 analyser was unable to accurately measure the fraction of CO_2 in the expired air during the heliox trial. Therefore data for VCO_2 and RER were measurable only in the normoxia and hyperoxia trials. Neither VCO_2max nor RERmax were different in these trials (VCO_2: normoxia = 5.3 ± 0.8 L.min^{-1}; hyperoxia = 5.3 ± 0.6 L.min^{-1}; RER: normoxia = 1.08 ± 0.03; hyperoxia = 1.07 ± 0.05). There is no reason to expect different results during exercise in heliox.

Figure 2 shows individual values for VO_2max, V_E and maximum power output. It is noticeable that whereas maximum values for VO_2max and $V_E$max varied by 6.2 and 7.8% respectively between the heliox and hyperoxia trials, the variation in maximum power output was substantially less (1.2%). This translates to an individual variation in maximum exercise performance of approximately 5 W corresponding to a difference in exercise time of 10 s.

Submaximum values of VO_2, VCO_2, V_E and RER

Figure 3 (top panels) shows changes in oxygen consumption and minute ventilation for the first 6 minutes of the exercise test in all 8 subjects. Thereafter there was progressive subject fallout so that complete data for all these measurements are not available after the first 6 minutes of exercise. Submaximum VO_2, VCO_2 and RER were not different in any of the conditions, whereas submaximum V_E was significantly lower ($p < 0.05$) from 270 to 360 seconds in the heliox trial compared with the normoxia trial ($p < 0.05$).

Figure 3 (bottom panels) shows these same variables but in the final 360 s preceding the point of exercise termination in all 8 subjects. These data show that neither VO_2 nor V_E were influenced by the nature of the gas mixture inhaled in the final 360 s of the trial.

Neither VCO_2 (top panel) nor RER (bottom panel) was different between hyperoxia and normoxia (Figure 4).

Incidence of the VO_2max plateau phenomenon

In accordance with the methods employed by Taylor et al (1955), we determined that the mean increase in oxygen uptake across two consecutive 30 s periods from 240 s to 90 s preceding fatigue (0 s) was 146.1 ± 75.2 $mL.min^{-1}$ (Figure 3 - bottom left panel), which is similar to the values found by Barstow et al (1996). Therefore an increase of less that 90 $mL.min^{-1}$ across two consecutive 30 s time periods was used as the criteria for defining a plateau in oxygen consumption. However to avoid the error of describing a plateau where none existed (Glassford et al, 1965), subjects were required to exhibit two consecutive increments in oxygen consumption of less than 90 $mL.min^{-1}$. Based upon these parameters the "plateau phenomenon" was exhibited by only one subject in the normoxia trial and by a different subject

during the heliox trial. Thus of 24 trials only 2 (8.3%) displayed a plateau phenomenon.

Heart Rate

Maximal heart rate was not different between conditions (normoxia = 180 ± 8 beats.min^{-1}; hyperoxia = 189 ± 6 beats.min^{-1}; heliox = 194 ± 4 beats.min^{-1}) and increased linearly as a function of workload (Figure 5 – top left panel).

Ratings of perceived exertion

There was no difference in the ratings of perceived exertion, which increased as a function of workload in all trials ($p < 0.05$) (Figure 5 – top right panel).

Lactate

Plasma lactate concentrations rose similarly in all trials (Figure 5 – bottom left panel). Maximum plasma lactate concentrations were not different between trials.

IEMG

Raw EMG data from the maximal ramp tests were normalised to the greatest MCV recorded before exercise and expressed as a percentage of the initial recording. There was no difference in the iEMG between the trials, although all increased as a function of workload ($p < 0.05$) (Figure 5 – bottom right panel).

Discussion

Our previous study (Nobbs et al, 2003) established that an F_IO_2 of 35% significantly increased arterial pO_2, oxygen saturation and haemoglobin saturation during the identical progressive exercise tests used in this study, compared to values measured during exercise in F_IO_2 of 21%. Hence our conclusion that the methods used in this study to produce a hyperoxic exercise environment did indeed cause a significant increase in arterial oxygen content.

Accordingly, the first important finding of this study was that maximum exercise performance was significantly increased in hyperoxia as a direct consequence of the increased arterial O_2 content although the exact mechanism by which this increase enhances performance remains uncertain. This agrees with the findings of a number of other carefully conducted studies (Adams et al, 1980; Hughson et al, 1995; Weltman et al, 1978; Wilson et al, 1975).

However, our study is the first to be conducted in a pressure-sealed chamber in which athletes inhaled the gas mixtures directly from the environment and not through variable and usually unspecified lengths of respiratory tubing necessary to provide the inspiratory gas from mixing bags. Thus, we conclude that the effects we measured resulted from the direct physiological effects of hyperoxia and were not due to a possible secondary interaction with the system through which the altered gas mixtures are delivered to the athlete.

The second important finding, which is entirely novel, was that exercise in hyperoxia was not associated with an increase in either submaximum (Figure 3) or maximum oxygen consumption (Figure 1 and 3), nor in the respiratory exchange ratio (Figure 5). Most previous studies have concluded that both the

submaximal and maximal VO_2max are increased in hyperoxia (Byrnes et al, 1984; Richardson et al, 1999a; Welch et al, 1974; Weltman et al, 1978). The finding that the maximum work rate increased without any increase in VO_2max confirms that the increased work rate was not the direct consequence of increased skeletal muscle oxygen consumption.

Indeed we too have also previously reported that under identical testing conditions but with the use of a different gas analysis system, both the submaximal and maximal VO_2max were significantly increased and RER significantly reduced in a similar group of subjects exercising in the same chamber with F_IO_2 of either 35 or 60% (Nobbs et al, 2003). However, since the sole difference between trials was the system used for gas analysis, we are inclined to the belief that the finding of an increased VO_2 during exercise in hyperoxia is more likely due to the technical difficulties in measuring VO_2 when F_IO_2 is increased above 21%, as has previously been proposed (Welch et al, 1981). We base this conclusion on four findings.

First, the original studies reported very large increases of up to 50% in VO_2 during exercise in hyperoxia (Furasawa, 1925; Hill et al, 1925). But as the instruments fro measuring VO_2 during exercise have improved, the magnitude of this effect has reduced substantially so that more modern studies find more modest VO_2max increases of 2 – 10% during exercise in hyperoxia (Hogan et al, 1983; Hughson et al, 1995). But, all such studies report a discrepancy in the magnitude of the changes in VO_2max and in the maximum work rate such that the increase in VO_2max is disproportionately large (Weltman et al, 1978). This discrepancy is difficult to understand since it implies that the extra work in hyperoxia is being achieved at a disproportionate cost; that is, that the human functions less economically when the F_IO_2 increases beyond 21%.

Second, if submaximum VO_2 increases in hyperoxia, as is usually found including our previous (Nobbs et al, 2003) but not this study (Figure 3), then the conclusion must be that VO_2 is suppressed during exercise in normoxia and that such suppression is exposed only by hyperoxia. It is difficult to predict the nature or physiological value of any suppression of the submaximum VO_2 during exercise in normoxia.

Third, RER in hyperoxia in the previous study (Nobbs et al, 2003) was significantly attenuated even from the start of exercise and this difference remained throughout exercise even at the maximum work rate. It is difficult to understand how hyperoxia should produce an intensity-independent change in metabolism in which fat oxidation is promoted and carbohydrate oxidation is suppressed beginning at rest (Adams et al, 1986). The biochemical basis for such suppression is not immediately apparent. Thus a more plausible explanation for these discrepant findings would seem to be that the majority of systems measuring respiratory gasses during exercise incorrectly measure VO_2 but not VCO_2 in hyperoxia but that the system used in this study may have provided the more accurate measurements of the real VO_2 during exercise in hyperoxia. By calculating VO_2 through numerical integration of the area under the curve of flow rate and F_EO_2 (Equation 1), the potential error associated with a decreasing inspiratory nitrogen fraction is eliminated in the hyperoxia and heliox conditions in this study (Hill et al, 1924b; Welch et al, 1981).

The fourth and most important finding of this study was that the substitution of helium for nitrogen in the hyperoxic gas mixture failed to alter exercise performance more than did hyperoxia alone. Furthermore, V_Emax was unaltered by either hyperoxia or by hyperoxia combined with helium enrichment. Thus unloading of the work of breathing failed to influence

exercise performance. This proves that the absolute respiratory muscle work is not the "exercise stopper" during maximal exercise in humans. This contrasts with findings in animals in which the J reflex inhibits muscle contraction following the activation of pulmonary C fibres (Gandevia et al, 2000).

Others have noted that V_E is not altered during exercise in a helium-enriched environment (Mancini et al, 1997), nor reduced in hyperoxia (Peltonen et al, 1995; Robbins et al, 1992; Weltman et al, 1978). Hence the suggestion that ventilation during exercise is not determined by either the work of breathing or the arterial oxygen content but may be linked to muscle mechanical work sensed by muscle mechanoreceptors (Babb, 2001) or perhaps the rate of CO_2 production by muscle.

The finding that the heliox mixture did not increase the maximum power output contrasts with findings in other studies in which the respiratory gasses were delivered through respiratory tubing from the gas bags in which gas mixing occurred (Babb, 1997a; Babb, 1997b; Esposito et al, 1997; Wilson et al, 1980). We interpret these contrary findings as evidence that neither inspiratory nor expiratory resistance influences exercise performance in healthy humans inhaling air directly from the environment and exhaling that air across the low resistance valves typical of the modern equipment used in this experiment.

In contrast, when the mixed gas is inspired through respiratory tubing of indeterminate length and airflow resistance and from gas bags in which mixing occurs, maximum exercise performance may be increased if the helium in the inspired gas reduces the (increased) inspiratory resistance present in these artificial systems used to deliver altered gas mixtures to the athletes (Johnson et al, 1996).

Indeed others have concluded that the healthy human respiratory tree does not cause a resistance sufficient to impair exercise performance (Babb, 1997a; Esposito et al, 1997). In contrast, increasing the external resistance to inspiration can significantly reduce maximum exercise performance in humans (Dressendorfer et al, 1977).

Indeed this latter finding proves that an unphysiological inspiratory resistance to airflow must be one of the "exercise stoppers". But our study shows that this may occur only in disease, since it was not present in our healthy young athletes even though they achieved very high rates of maximum ventilation (~160 $L.min^{-1}$). Thus the afferent sensory pathways directing this inhibitory effect on exercise performance are likely to be active only in persons with obstructive lung disease or cardiac failure in whom the substitution of helium for nitrogen in the inspired gas mixture does indeed improve maximal exercise performance (Mancini et al, 1997; Richardson et al, 1999b). This effect would perhaps act via a supposed central controller or governor that limits the recruitment of additional motor units in order to preserve homeostasis during maximal exercise (Noakes et al, 2001)

However, even though $V_E max$ was not altered in either hyperoxia or in the heliox condition, submaximum V_E was indeed significantly decreased during exercise in heliox (Figure 3). Thus a component of the stimulus for ventilation at low work rates can be altered by reducing the work of breathing although, not by hyperoxia alone. However, once the exercise intensity increases, this effect is lost. Since hyperoxia did not alter the ventilatory response to exercise, it appears that the control of ventilation during exercise must involve either feedforward control or the coupling of respiratory muscle work with skeletal muscle work (Babb, 2001), perhaps through the rate of CO_2 production. Indeed the finding that exercise in heliox also did not reduce

V_E confirms the findings of Babb (2001) and support his interpretation that the level of skeletal muscle work may determine the ventilatory response to exercise.

But since absolute respiratory muscle work was clearly not an "exercise stopper" in this study, it raises the question of exactly why the subjects terminated exercise in both hyperoxia and in the heliox condition. The popular theory that an oxygen deficiency limits maximal exercise performance is based on the erroneous interpretation of A.V. Hill and colleagues' original studies (Noakes, 1988; Noakes, 1997)and the assumption that these researchers proved that a "plateau" in oxygen consumption identifies the development of skeletal muscle anaerobiosis.

Others have presented evidence to show that the plateau phenomenon may be an artefact of the testing protocol and the methods used to measure VO_2, rather than a valid index of skeletal muscle anaerobiosis (Myers et al, 1989). However, the important finding in this study was that only two of 24 tests (8%) showed evidence for a "plateau" and these occurred in two different individuals. Hence we conclude that even according to the potentially erroneous concept of the "plateau phenomenon", the development of a true oxygen deficiency could not have been an "exercise stopper" in any but a tiny minority of tests in this study, as also found in our previous study (Nobbs et al, 2003). Indeed the incidence of the plateau phenomenon in this study was the lowest yet reported in the literature. The use of the ramp protocol might explain the near absence of this "phenomenon" in this and other studies (Myers et al, 1989).

Although a rising muscle lactate concentration has usually been considered an important "exercise stopper", the findings of Nielsen et al (Nielsen et al, 2001) and Posterino et al (Posterino et al, 2001) do not support that theory. Both

studies failed to find any evidence that elevated muscle lactate concentration acts as an "exercise stopper" Indeed, in this study, blood lactate concentrations were not influenced by any of the interventions that were studied. This contrasts with the usual belief that hyperoxia improves performance by reducing muscle and blood lactate concentrations as a result of a reduced skeletal muscle anaerobiosis (Linossier et al, 2000). Arterial pH measured at exhaustion under identical conditions was only mildly acidotic (Nobbs et al, 2003) and arterial pO_2 was high. Hence it is unlikely that a reduced pH or pO_2 causes exercise termination although the higher arterial pO_2 in hyperoxia may have been the direct stimulus allowing a higher work rate according to the Central Governor theory (Noakes et al, 2001).

More to the point, we were surprised at the very small variation in peak work rate in hyperoxia and in hyperoxia with helium (Figure 2). The coefficient of variation within peak work rates was 1.2%, equivalent to a work rate of 5 W and exercise duration of 10 seconds. In contrast the variation in peak VO_2max was 6.2%. Thus it appears as if the peak work rate itself, acting as part of a neural reflex, might have been an "exercise stopper" since it is difficult to imagine any other than a neural reflex that could produce such a close matching of the peak achieved work rates in the hyperoxic and heliox conditions, in tests conducted up to 7 days apart. Such a mechanoreceptor reflex would act similarly to the J reflex in animals.

In conclusion, this study confirms that hyperoxia increases the work rate at which progressive exercise to exhaustion terminates (Nobbs et al, 2003). However, the addition of unloading respiratory muscle work during exercise in a helium- and oxygen-enriched environment did not enhance performance more than did hyperoxia alone. This proves that the absolute amount of respiratory muscle work is not the "exercise stopper" in humans as it is in

other mammals (Gandevia et al, 2000). In contrast, the tight coupling of absolute ventilation to work rate in both hyperoxia and hyperoxia with helium (Figure 3 – right panel), the remarkable similarity (~5 W) of the higher "stopping" work rate in both hyperoxia and hyperoxia with helium (Figure 1 and Table 1), the significant increase in peak work without an equivalent increase in VO_2max, and the absence of evidence that exercise terminated as a result of skeletal muscle anaerobiosis, supports an alternative hypothesis that afferent information from the mechanoreceptors in the exercising skeletal muscles may act as the "exercise stopper" during progressive maximal exercise to exhaustion. Alternatively, the maximal extent of motor unit recruitment during exercise may be hardwired in the central nervous system in a system of feed-forward control and may be influenced to only a small extent by the interventions evaluated in this trial and which simultaneously increased the potential for oxygen delivery to the muscles and reduced respiratory muscle work during progressive maximal exercise to exhaustion.

LEGEND TO FIGURES

Figure 1 Maximal values of power output, VO_2 and V_E attained during maximal exercise in a sealed pressure chamber performed under normoxic, hyperoxic and heliox conditions.

* Normoxia is significantly different from hyperoxia and heliox trials ($p < 0.05$)

Figure 2 Comparison of individual peak power output, VO_2 and V_E for each subject during maximal exercise in a sealed pressure chamber under normoxic (■), hyperoxic (▩) and heliox (□) conditions.

Figure 3 (Upper) Submaximal VO_2 and V_E for the initial 360 s of maximal exercise in a sealed pressure chamber performed under normoxic (•), hyperoxic (x) and heliox (O) conditions.

* Heliox is significantly different from normoxia ($p < 0.05$)

λ Heliox is significantly different from normoxia and hyperoxia ($p < 0.05$)

Figure 3 (Lower) VO_2 and V_E for the final 330 s of maximal exercise in a sealed pressure chamber performed under normoxic (•), hyperoxic (x) and heliox (O) conditions.

Figure 4 Submaximal VCO_2 and RER for the initial 360 s of maximal exercise in a sealed pressure chamber performed under normoxic (•) and hyperoxic (□) conditions.

Figure 5 Submaximal and maximum heart rate, RPE, plasma lactate concentrations and iEMG during maximal exercise in a sealed pressure chamber performed under normoxic (•), hyperoxic (x) and heliox (O) conditions.

TABLE 1

Maximal values for power output, VO_2, V_E and VCO_2 during maximal exercise in a sealed pressure chamber under normoxic, hyperoxic and heliox conditions.

	Normoxia 21% O_2	Hyperoxia 35% O_2	Heliox 35% O_2:65% He
Wmax (W)	429 ± 56	451 ± 58	454 ± 56
VO_2max ($L.min^{-1}$)	4.9 ± 0.7	5.0 ± 0.6	4.9 ±0.7
$V_E$max ($L.min^{-1}$)	155 ± 24	157 ± 24	163 ± 22
VCO_2max ($L.min^{-1}$)	5.3 ± 0.8	5.3 ± 0.6	N/A

N/A = not available. VCO_2 could not be measured in the heliox condition.

FIGURE 1

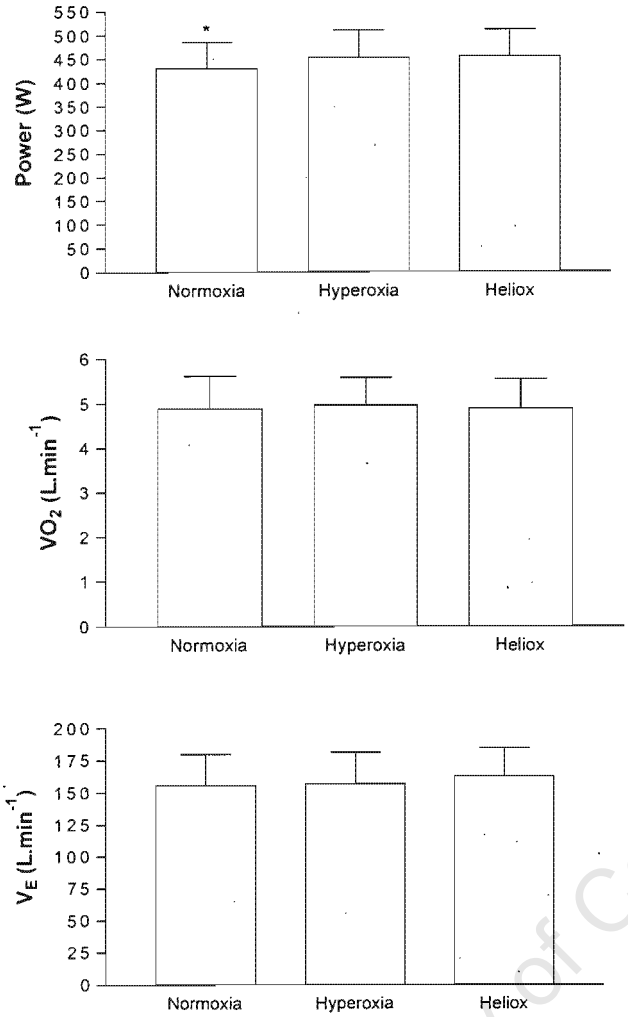


FIGURE 2

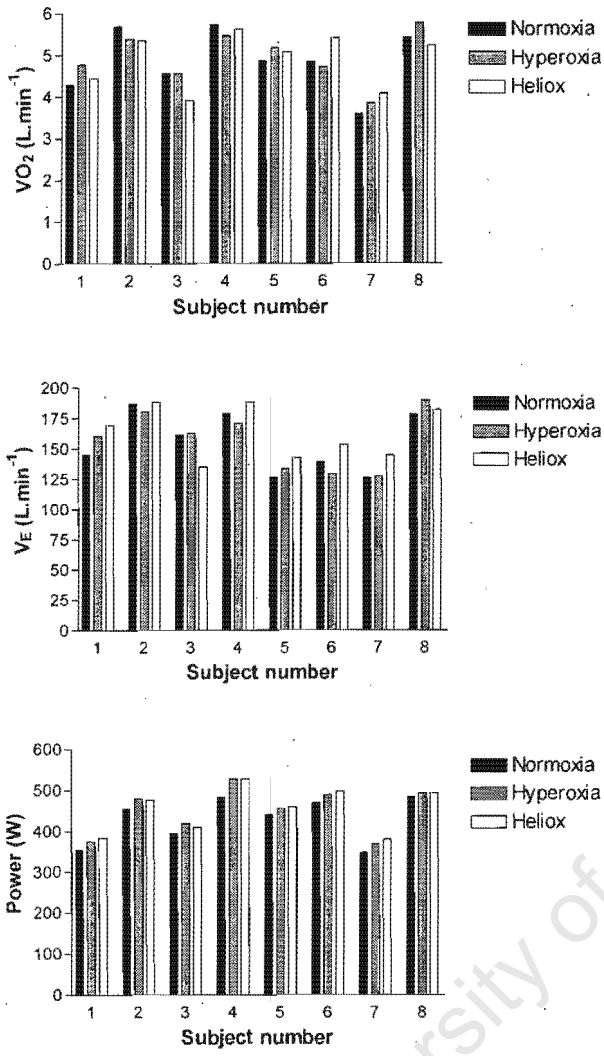
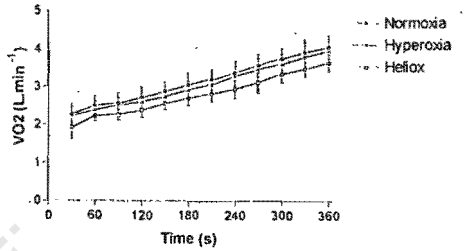
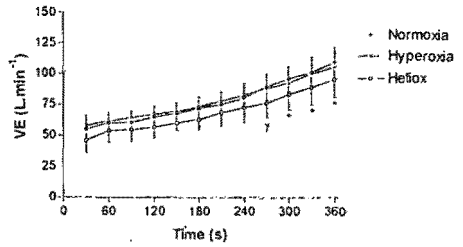
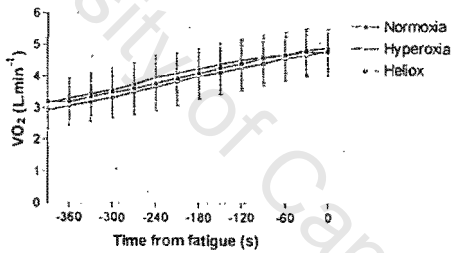


FIGURE 3







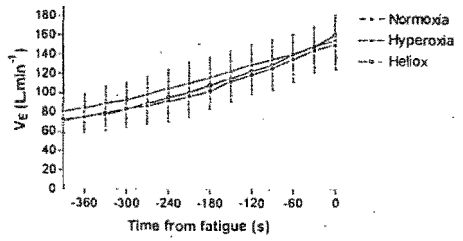
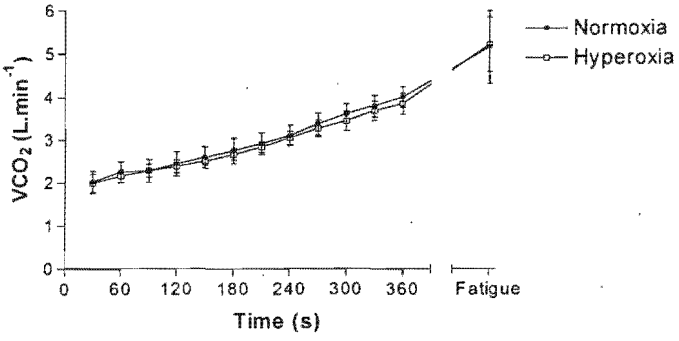


FIGURE 4



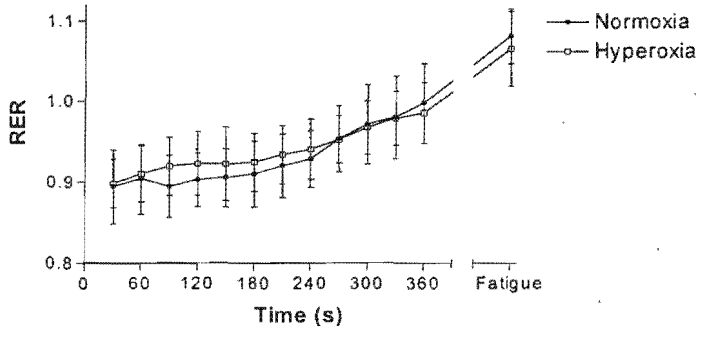
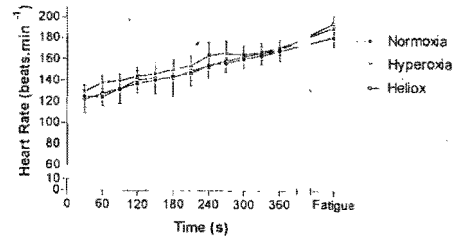
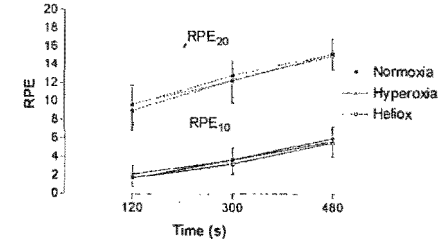
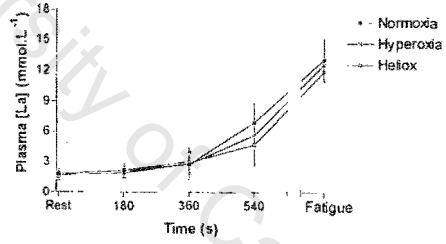
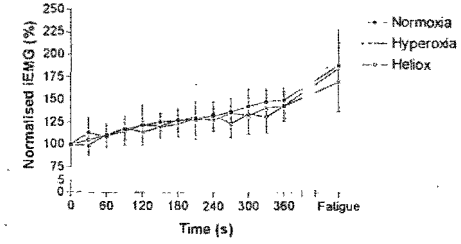


FIGURE 5









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