Optimising Exercise Intensity Prescription to Reduce Adaptive Variability Following High-Intensity Interval Training

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Declaration

I, Arthur Henrique Souza Neto Bossi, declare that no part of this thesis has been submitted in support of an application for any degree or other qualification of the University of Kent, or any other University or Institution of learning.

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Abstract

The aim of this thesis was to optimise intensity prescription for high-intensity interval training (HIIT), ultimately enhancing the magnitude of the training stimulus, and reducing inter-individual variability in adaptive responses. In Chapter 4, it was demonstrated that %Δ, a method wherein maximal and submaximal performance determinants are considered to prescribe exercise intensity, elicits large inter- and intra-individual variability in performance, physiological, and perceptual responses to HIIT. In Chapter 5, the large inter-individual variability observed in Chapter 4 was reproduced when %Δ and other methods of intensity prescription were tested, including percentage of maximal oxygen uptake, percentage of maximal work rate in an incremental test (%$\dot{W}_{max}$), percentage of average work rate sustained in a 20-min time-trial, and percentage expenditure of work capacity above critical power. In Chapter 6, it was demonstrated that prescribing HIIT with work intervals of variable power output may maximise the cardiorespiratory stress of training without incurring additional effort (quantified by ratings of perceived exertion) or metabolic stress (quantified by blood lactate concentration). In Chapter 7, it was demonstrated that most training sessions are completed by participants training at their maximal sustainable work rate, whereas sessions performed at 80%$\dot{W}_{max}$ are often interrupted prematurely due to exhaustion, despite a similar training intensity on average. It was also demonstrated that the magnitude of inter-individual variability in adaptive responses, although only detected for maximal oxygen uptake and self-paced HIIT performance, was not influenced by how training intensity was prescribed. There were no prescription method effects on mean adaptive responses. Overall, this thesis questions some intensity prescription methods used for HIIT, provides evidence that varying power output during work intervals may maximise training stimulus, demonstrates that a maximal self-paced performance may be used as an intensity prescription benchmark, and challenges the belief that how training intensity is prescribed/normalised affects adaptive response variability.

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$$\dot{V}O_2 = \dot{Q} \cdot a\text{-}\bar{v}O_{2diff} \quad (2.1)$$

$$a\text{-}\bar{v}O_{2diff} = CaO_2 \times \bar{O}_{2extrac} \quad (2.2)$$

Chapter 4 – The delta concept is not a valid method to normalise the intensity of exhaustive interval training

$$\dot{W}_{target} = \dot{W}_{GET} + [(\dot{W}_{\dot{V}O2max} - \dot{W}_{GET}) \cdot \%\Delta] \quad (4.1)$$

Chapter 5 – Current methods to prescribe exercise intensity are inappropriate for exhaustive interval training

$$\dot{W}_{target} = (W' \cdot 0.8)/240 + CP) \quad (5.1)$$

$$CV\ (\%) = \sqrt{(e^{Var\text{-}1})} \quad (5.2)$$

Chapter 6 – Optimizing interval training through power output variation within the work intervals

$$\Delta\dot{V}O_2\ (ml) = 23.3 \cdot \Delta\dot{V}E\ (L \cdot min^{-1}) + 239.6 \quad (6.1)$$

Chapter 1 – Introduction

1.1 – Background

The repeated exposure to the homeostatic perturbation associated with each exercise session of a training programme, over time, leads to physiological adaptations that improve physical performance (Egan and Zierath, 2013, Flück, 2006, Hawley et al., 2014, Perry et al., 2010). This suggests that training programmes should be carefully planned in terms of frequency, duration, and intensity, as these variables determine the exercise dose (Garber et al., 2011, Howley, 2001). While frequency and duration are rather intuitive (e.g. 5 sessions per week lasting 60 min each), the prescription of intensity in absolute terms (e.g. 150 W) is not recommended, given that the cardiorespiratory and metabolic demand elicited by a certain exercise rate, and by consequence, the homeostatic perturbation, is influenced by the individual's physiological capacity (Garber et al., 2011, Howley, 2001).

Customarily, endurance exercise intensity has been expressed in relative terms, normalised across individuals as a fraction of their maximal oxygen uptake (%$\dot{V}O_{2max}$) (Howley, 2001, Jamnick et al., 2020, Mann et al., 2013). The rationale for this choice reflects long-established work reporting a) that time to complete an endurance task was inversely associated with the maximal oxygen uptake ($\dot{V}O_{2max}$) (Costill et al., 1973, Herbst, 1928), and b) that the magnitude of some physiological responses to exercise, such as cardiac output and blood lactate concentration ([La^-]), was a function of the %$\dot{V}O_{2max}$ elicited (Åstrand et al., 1964, Costill, 1970). More recently, however, it has become clear that $\dot{V}O_{2max}$ alone does not predict endurance performance in a group of homogeneous athletes (Conley and Krahenbuhl, 1980, Coyle et al., 1988, Lacour et al., 1990). Moreover, it is now understood that characterising exercise based on intensity domains, rather than %$\dot{V}O_{2max}$, allows for more predictable profiles of gas exchanges, blood acid-base balance, and intramuscular phosphagen status (Jamnick et al., 2020, Rossiter, 2011). Accordingly, there have been several findings that challenge the %$\dot{V}O_{2max}$ approach, suggesting it should not be used for exercise intensity prescription (Jamnick et al., 2020, Mann et al., 2013).

In one of these studies, Coyle et al. (1988) investigated time to exhaustion (TTE) at 88%$\dot{V}O_{2max}$ in two groups of well-trained cyclists of similar $\dot{V}O_{2max}$, but with lactate threshold occurring at different %$\dot{V}O_{2max}$. TTE averaged 61 and 29 min, and post-exercise [La^-] averaged 7.4 and 14.7 $mmol \cdot L^{-1}$, for groups of high (82%$\dot{V}O_{2max}$) and low (66%$\dot{V}O_{2max}$) lactate threshold, respectively. Although Coyle et al. (1988) provided evidence against the use of %$\dot{V}O_{2max}$ for intensity normalisation, it was not the aim of the study to

compare %$\dot{V}O_{2max}$ with a different method. While other authors have done this comparison (Baldwin et al., 2000, Barnett et al., 1996, Blondel et al., 2001, Egger et al., 2016, Iannetta et al., 2020, Lansley et al., 2011, McLellan and Jacobs, 1991, McLellan and Skinner, 1985), some uncertainty remains. For example, there have been contradictory findings on the delta concept (%Δ), in which gas exchange (GET)/lactate threshold as well as $\dot{V}O_{2max}$ are considered to normalise exercise intensity (Lansley et al., 2011, McLellan and Gass, 1989, McLellan and Skinner, 1985). While %Δ may be considered superior to %$\dot{V}O_{2max}$ for its ability to minimise inter-individual variability in exercise responses (Lansley et al., 2011, McLellan and Skinner, 1985), this method has been shown not to produce equivalent metabolic and cardiorespiratory stress in two groups of similar $\dot{V}O_{2max}$ but different lactate threshold when exercise was performed at 67%Δ (McLellan and Gass, 1989). As another example of discord, it has been shown that maximal values alone (e.g. %$\dot{V}O_{2max}$, percentage of maximal work rate in an incremental test (%$\dot{W}_{max}$), or percentage of maximal heart rate (%HR_{max})) fail to produce homogeneous exercise responses across individuals (Egger et al., 2016, Iannetta et al., 2020), although contrasting findings suggest %$\dot{W}_{max}$ may be of use in certain situations (Bentley et al., 2007a). It is worth mentioning that inter-individual variability in physiological responses tends to escalate as exercise intensity increases, at least for prescriptions based on %$\dot{V}O_{2max}$ (Scharhag-Rosenberger et al., 2010). It is therefore conceivable that the ideal method might be intensity-domain dependent, which would partly explain the lack of consensus. Overall, these studies suggest exercise physiologists have yet to determine a robust approach for exercise intensity normalisation that encompasses the whole spectrum of training intensities.

Despite the evidence that traditional methods of exercise intensity prescription may produce a range of exercise responses across individuals, they continue to be used, even in studies that investigated inter-individual variability in adaptive responses to an exercise programme (Astorino and Schubert, 2014, Bonafiglia et al., 2016, Bouchard et al., 1999, Coakley and Passfield, 2018b, Del Giudice et al., 2020, Hecksteden et al., 2018b, Maturana et al., 2021, Montero and Lundby, 2017, Ross et al., 2015, Vollaard et al., 2009, Weatherwax et al., 2019, Williams et al., 2019). Intensity prescriptions have been normalised mostly based on %$\dot{V}O_{2max}$ (Bonafiglia et al., 2016, Bouchard et al., 1999, Ross et al., 2015, Vollaard et al., 2009), %$\dot{W}_{max}$ (Astorino and Schubert, 2014, Coakley and Passfield, 2018b, Montero and Lundby, 2017), %HR_{max} (Del Giudice et al., 2020, Maturana et al., 2021, Williams et al., 2019), and percentage of heart rate reserve (%$HR_{reserve}$) (Hecksteden et al., 2018b,

Weatherwax et al., 2019), indicating that participants may have not received the same training stimulus. Accordingly, the lack of consistency with which each participant experienced cardiorespiratory and metabolic stress through training may explain the heterogeneous adaptive responses observed (Iannetta et al., 2020, Mann et al., 2014, Meyler et al., 2021). In contrast, when a consistent training stimulus is provided (i.e. all exercise sessions are performed to exhaustion), inter-individual variability in adaptive response is minimal as evidenced by Hickson et al. (1977). In this 10-week training study, untrained individuals exercised for 40 min per day, six days per week. On alternate days, three sessions were performed as high-intensity interval training (HIIT) on a cycle ergometer (i.e. 5-min work intervals that elicited $\dot{V}O_{2max}$, interspersed with 2-min active recovery) and three sessions were performed as 40-min time-trials on a treadmill. As shown in Figure 1.1, $\dot{V}O_{2max}$ increased quasi-linearly throughout the study, and there was little inter-individual variability in the slope of regression lines of $\dot{V}O_{2max}$ over time. As a whole, the evidence indicates that methodological choices may be a fundamental source of inter-individual variability in training adaptations (Mann et al., 2014, Meyler et al., 2021).

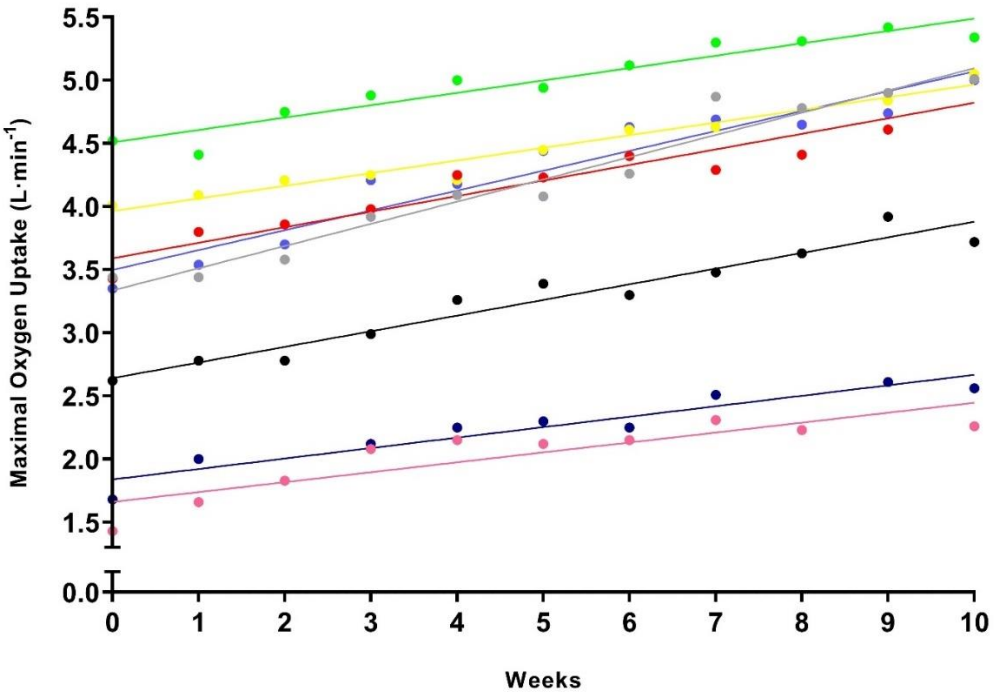

Figure 1.1 – Maximal oxygen uptake over time from Hickson's training study (Hickson et al., 1977). Each colour represents an individual. Best-fitting lines were derived by the least-squares method.

1.2 – The problem with HIIT

A quick literature search reveals that HIIT has received much less attention than continuous exercise when it comes to the normalisation of exercise intensity, with few studies evaluating the effectiveness of alternative intensity prescription methods (Astorino et al., 2018, Bartram et al., 2018, Ferguson et al., 2013, Julio et al., 2020, Nicolò et al., 2014). This is at odds with the great popularity of HIIT, often considered superior to continuous exercise in improving physiological function and exercise capacity (Bacon et al., 2013, Laursen and Jenkins, 2002, Midgley et al., 2006, Milanovic et al., 2015, Wen et al., 2019). While the notion of relative intensity may be considered a basic concept for endurance exercise prescription, the widespread use of normalisation methods of questionable effectiveness represents a serious limitation that may have biased the literature on adaptive variability (Astorino and Schubert, 2014, Bonafiglia et al., 2016, Bouchard et al., 1999, Coakley and Passfield, 2018b, Del Giudice et al., 2020, Hecksteden et al., 2018b, Maturana et al., 2021, Montero and Lundby, 2017, Ross et al., 2015, Vollaard et al., 2009, Weatherwax et al., 2019, Williams et al., 2019). This is especially important in the context of HIIT-based interventions (Astorino and Schubert, 2014, Bonafiglia et al., 2016, Coakley and Passfield, 2018b, Del Giudice et al., 2020, Maturana et al., 2021, Williams et al., 2019), for which researchers have yet to test the effectiveness of all available methods of intensity prescription (Astorino et al., 2018, Bartram et al., 2018, Ferguson et al., 2013, Julio et al., 2020, Nicolò et al., 2014). Therefore, further investigations must be conducted, and new methods should, perhaps, be developed. Ultimately, more research effort should be devoted to the methodological aspect of training in order to advance our understanding of adaptive variability.

Chapter 2 – Literature review

2.1 – Background

Performance during endurance exercise can be defined in several ways. For instance, a) time to cover a fixed distance, b) distance covered in a fixed time, c) average work rate to complete a fixed distance or time, and d) TTE at a fixed or increasing work rate. Usually, options a, b, and c are referred to as time-trials, whereas option d is called TTE test or incremental test whether the work rate is respectively fixed or incremental. Although the ideal test may be context-dependent and subject to disagreement (Amann et al., 2008, Black et al., 2015, Coakley and Passfield, 2018a, Currell and Jeukendrup, 2008, Hopkins et al., 2001), generally, the purpose of training is to increase performance through the completion of systematic and regular exercise sessions.

Throughout most of the sports' history, the training process has been guided by intuition as a matter of trial and error (Krüger, 2006, Vettenniemi, 2012). Not many decades ago, the most sophisticated training instrument available was the stopwatch. However, with an increase in the number of scientific publications on exercise physiology following the inception of the Harvard Fatigue Laboratory in 1927 (Table 2.1), the training process has become progressively more scientifically grounded over subsequent decades. Indeed, Eliud Kipchoge recently broke the world record for the men's marathon (2 h 01 min 39 s, Berlin, Germany, 2018), while Brigid Kosgei broke the world record for the women's marathon (2 h 14 min 04 s, Chicago, USA, 2019). Notably, Kipchoge also recorded 1 h 59 min 40 s for the marathon distance in an exhibition event (Vienna, Austria, 2019) not sanctioned by the International Association of Athletics Federations. Although the use of banned performance-enhancing drugs may be linked to exceptional performances (Coyle, 2013), it is the view of many physiologists that these new records represent not only the combination of outstanding physiological attributes and technological advancement, but also the impact of current scientific support to training, nutrition, and racing (Joyner et al., 2020).

Table 2.1 – Events that led to the establishment of exercise physiology as a discipline.

Year	Event
1900	Exercise physiology and related textbooks printed up to 1935 listed no more than 28 citations from studies published before 1900.
1923	The concept of maximal oxygen uptake was described by Hill and Lupton (1923).
1927	The Harvard Fatigue Laboratory was established.
1931	Bock and Dill's textbook The Physiology of Muscular Exercise by the Late F.A. Bainbridge (Bock and Dill, 1931) listed more than 420 citations.
1947	The Harvard Fatigue Laboratory was closed after 316 peer-reviewed articles and 3 books published, in which 20% of the overall publication record was exercise physiology-related.
1948	The Journal of Applied Physiology was established.
1954	The American College of Sports Medicine was established.
1960	Johnson's textbook Science and Medicine of Exercise and Sport (Johnson, 1960) listed more than 1000 citations.
1964	The National Institute of Health created the Applied Physiology Study Section to fund research related to exercise physiology.
1969	The Medicine and Science in Sports was established, later renamed Medicine and Science in Sports and Exercise.
1970	Åstrand and Rodahl's Textbook of Work Physiology (Åstrand and Rodahl, 1970) listed more than 900 citations.
1971	The first Department of Exercise Science is established at the University of Massachusetts.
1977	The American Physiological Society created a membership section entitled Environmental, Thermal, and Exercise Physiology, later renamed Environmental and Exercise Physiology.

Information compiled from Tipton (1998).

One might think, therefore, that science has produced major breakthroughs that altered the training paradigm in force at the time of discovery. However, this interpretation is far from true (Bishop, 2008). More often, scientists have just confirmed from a physiological point of view what athletes and coaches had already learnt through their practice (Billat, 2001, Hawley et al., 1997). Despite the large volume of literature supporting a scientific approach to endurance training (Figure 2.1), key knowledge gaps still exist, which may preclude scientists from exerting a more prominent role in the support of athletes. The following sections will provide context for the experimental chapters by highlighting the areas where the scientific literature is limited.

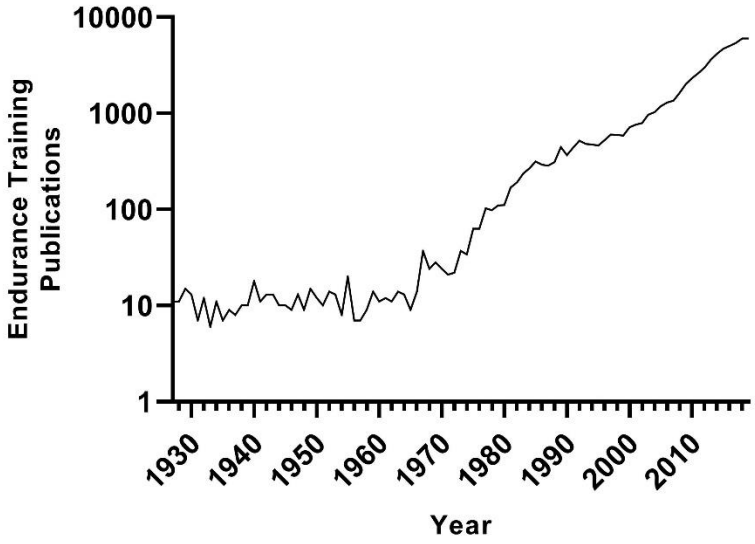

Figure 2.1 – Endurance training publications per year according to the Europe PMC database (http://europepmc.org).

2.2 – Performance model

The first step in the prescription of a training programme is to determine the physiological parameters that regulate exercise performance. Once these are established, training can be structured to maximise the function of the organs and tissues that govern these parameters. Hence, this section will focus on the physiological determinants of endurance performance according with the most accepted cardiovascular/anaerobic model (Abbiss and Laursen, 2005, Noakes, 2000). While other models exist to explain performance and fatigue (Abbiss and Laursen, 2005, Noakes, 2000), it is beyond the scope of this thesis to appraise all of them. It is important to note, however, that endurance performance is complex and unlikely to be satisfactorily described by a single model. Besides, for the purposes of this literature review, it is assumed optimal environmental conditions that do not add extra challenges to the normal physiological function (i.e. exercise performed at sea level, under thermoneutral temperatures and moderately dry air).

The cardiovascular/anaerobic model (Figure 2.2) implies that endurance performance can be predicted with an acceptable degree of precision once $\dot{V}O_{2max}$, fractional utilization of $\dot{V}O_{2max}$, gross mechanical efficiency, and anaerobic capacity of an individual are known (Bassett Jr. and Howley, 2000, Coyle, 1995, Joyner and Coyle, 2008). This model has been the most accepted to describe a) the aetiology of fatigue during endurance exercise, b) how

endurance exercise training promotes physiological adaptations, and c) how these adaptations improve exercise performance/capacity. It also provides the physiological framework for the design of effective training programmes. Some key limitations of this model include its inability to take into account changes in profiled variables over time as exercise continues (Maunder et al., 2021), and the absence of a role for the brain despite the evidence that endurance performance is at least partially regulated by the central nervous system (Noakes, 2011).

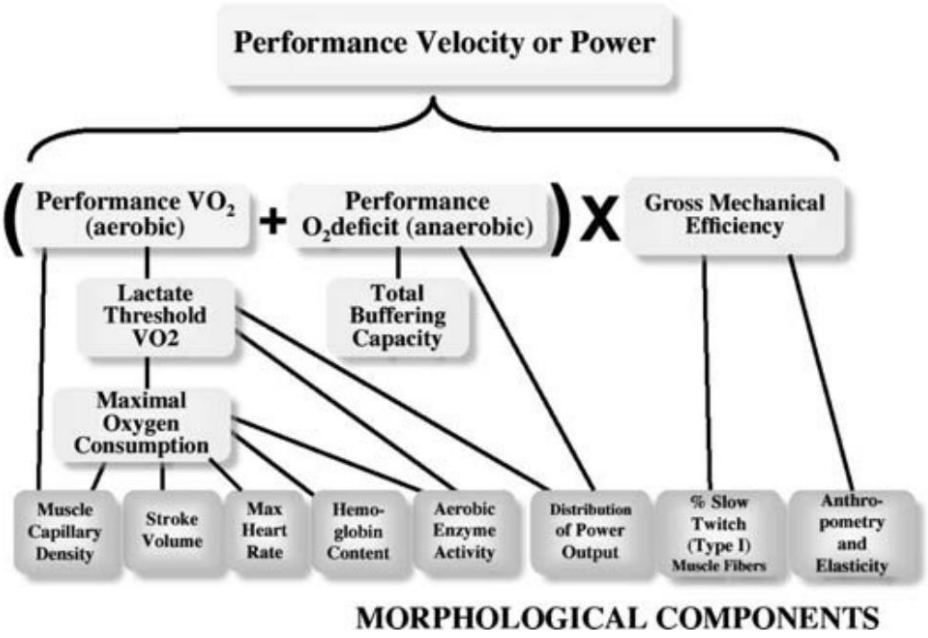

Figure 2.2 – Schematic representation of the endurance performance model as described by Joyner and Coyle (2008). Taken from Joyner and Coyle (2008) p. 37.

Although $\dot{W}_{max}$, GET, respiratory compensation point (RCP), critical power (CP) and work capacity above CP (W'), magnitude of the slow component of oxygen uptake ($\dot{V}O_2$) kinetics, fatigue resistance (i.e. contractile properties of skeletal muscle), substrate availability, or susceptibility to arterial desaturation and respiratory muscle fatigue may also be linked to endurance performance (Amann, 2012, Fitts, 1994, Hawley, 1995, Jones and Vanhatalo, 2017, Lucia et al., 2001, Sjödin and Svedenhag, 1985), these and other variables may be considered of secondary importance, or another representation of the physiological factors that comprise the cardiovascular/anaerobic model. For instance, it may be argued that the $\dot{V}O_2$ associated with CP would be a more relevant determinant of performance $\dot{V}O_2$ than the lactate threshold $\dot{V}O_2$ (Florence and Weir, 1997, Poole et al., 2021, Santos-Concejero et al.,

2020). This is because the latter represents the highest intensity before the glycolytic flux is markedly increased (Joyner and Coyle, 2008, Joyner et al., 2020, Poole et al., 2021), whereas the former represents the highest sustainable metabolic rate above which exercise leads to rapid functional deterioration and, ultimately, exhaustion (Jones et al., 2019, Poole et al., 2021, Rossiter, 2011). While it is acknowledged that the cardiovascular/anaerobic model may require some updates, it still provides a valid framework for the design of endurance training programmes.

2.2.1 – $\dot{V}O_{2max}$

$\dot{V}O_{2max}$ is one of the most common measures in exercise physiology. It represents the integrated capacity of the pulmonary, cardiovascular, and muscular systems to respectively uptake, transport, and utilize oxygen (Poole and Jones, 2017, Wagner, 2000). In other words, there exists for each person a maximal rate of oxygen that can be transported from the environment through the body to supply the mitochondria that support the ongoing contractile activity. As the relationship between $\dot{V}O_2$ and exercise work rate follows an approximately linear relationship (Hansen et al., 1988, Iannetta et al., 2019a), $\dot{V}O_{2max}$ has been used as an index of cardiorespiratory fitness/work capacity for both the general population (Kaminsky et al., 2015, Loe et al., 2013) and athletes (Haugen et al., 2018, Saltin and Astrand, 1967). Generally speaking, the higher the $\dot{V}O_{2max}$ of an individual is, the higher it is the individual's capacity to perform intense endurance exercise. Thus, $\dot{V}O_{2max}$ has been the preferred measure of many physiologists to demonstrate a training effect.

The concept of $\dot{V}O_{2max}$ as it is known today was first described by Hill and Lupton (1923). They performed a series of running experiments on an 85-m grass track to demonstrate the difference between steady-state exercise, whereby a constant $\dot{V}O_2$ was maintained after approximately 2 min at 11 and 12 $km \cdot h^{-1}$, and exercise that incurs an "oxygen deficit", whereby $\dot{V}O_2$ took longer to stabilise at 16 $km \cdot h^{-1}$, and a ceiling was attained (i.e. $\dot{V}O_{2max}$). Hill and Lupton (1923) also contrasted the highest $\dot{V}O_2$ recorded by other researchers with their well-substantiated maximal measures in five individuals, and, for the first time, a $\dot{V}O_{2max}$ relative to body mass was mentioned for the purposes of inter-individual comparison (i.e. current practice). In the following year, Hill et al. (1924) published another dataset evidencing an approximately linear relationship between running speed and $\dot{V}O_2$ that levels off at the highest speeds, which they interpreted as an indication of $\dot{V}O_{2max}$ attainment. A few decades later, Åstrand and Saltin (1961) confirmed that a $\dot{V}O_2$ ceiling was attained at a

range of work rates that led motivated individuals to give up cycling in between 3 to 6 min. Following this well-controlled laboratory study (Åstrand and Saltin, 1961) and others (Draper et al., 2003, Hill et al., 2002), it has now become clear that no $\dot{V}O_2$ rise beyond $\dot{V}O_{2max}$ is possible as the work rate of constant-intensity exercise bouts is progressively increased.

Given the technology available in the 1920's, Hill and colleagues (Hill et al., 1924, Hill and Lupton, 1923) were indeed pioneers. They correctly identified that constraints of the cardiorespiratory system prevent an infinite rise of $\dot{V}O_2$ and deduced some determinants of $\dot{V}O_{2max}$, based on the limited data available at the time, and knowledge of the Fick equation (Fick, 1870):

$$\dot{V}O_2 = \dot{Q} \cdot a\text{-}\bar{v}O_{2diff} \quad (2.1)$$

where $\dot{Q}$ is cardiac output and $a\text{-}\bar{v}O_{2diff}$ is arterial to mixed venous oxygen difference. Hill and colleagues (Hill et al., 1924, Hill and Lupton, 1923) believed that the maximal cardiac output ($\dot{Q}_{max}$) would play a major role in determining $\dot{V}O_{2max}$, which is now a well-established notion (Montero et al., 2015b, Skattebo et al., 2020). Given that maximal heart rate (HR_{max}) does not change much between trained and untrained individuals (Gledhill et al., 1994, Rowell, 1969, Saltin, 1969), the highest $\dot{V}O_{2max}$ (Haugen et al., 2018, Saltin and Astrand, 1967) and $\dot{Q}_{max}$ (Ekblom and Hermansen, 1968, Gledhill et al., 1994) attained by athletes result mainly from an increased stroke volume (Ekblom and Hermansen, 1968, Gledhill et al., 1994, Skattebo et al., 2020).

The Fick equation (Fick, 1870) also indicates that $a\text{-}\bar{v}O_{2diff}$, representing the ability of the muscles to extract oxygen from the perfusing blood, is a potential limiter of $\dot{V}O_{2max}$. Interestingly, Hill and Lupton (1923) predicted that an oxygen diffusion limit within the active muscle fibres would be attained during exercise at $\dot{V}O_{2max}$. This is consistent with the current view that a large oxygen extraction, secondary to an enhanced muscle oxygen-diffusing capacity, mitochondrial mass, and capillary density (Brodal et al., 1977, Jacobs and Lundby, 2013, Montero et al., 2015a, Richardson et al., 1995), contributes to a high $\dot{V}O_{2max}$ (Skattebo et al., 2020). However, it has been reported relatively small differences in $a\text{-}\bar{v}O_{2diff}$ between active male and female young adults (Åstrand et al., 1964), and no differences between well-trained and elite athletes (Ekblom and Hermansen, 1968), despite

large group differences in $\dot{V}O_{2max}$. Indeed, by compiling the data of several published studies (n = 154), Skattebo et al. (2020) have demonstrated an inverse J-shaped relationship between a-$\overline{v}O_{2diff}$ and absolute $\dot{V}O_{2max}$, which may be viewed as evidence that peripheral factors contribute minimally to a high $\dot{V}O_{2max}$. Such a conclusion is misguided, though, because it fails to account for the influence of endurance training on the determinants of a-$\overline{v}O_{2diff}$:

$$a\text{-}\overline{v}O_{2diff} = CaO_2 \times \overline{O}_{2extrac} \quad (2.2)$$

where CaO_2 is arterial oxygen content and $\overline{O}_{2extrac}$ is systemic oxygen extraction fraction. As endurance training triggers an expansion of plasma volume (Convertino, 1991), which might result in haemodilution and lower oxygen-carrying capacity of the arterial blood (Ekblom et al., 1968, Thirup, 2003), a higher $\dot{V}O_{2max}$ may be associated with a lower CaO_2, consequently concealing any increase in $\overline{O}_{2extrac}$ (Skattebo et al., 2020). This explains why the magnitude of changes in maximal a-$\overline{v}O_{2diff}$ following endurance training is typically inferior to the magnitude of changes in $\dot{Q}_{max}$ (Ekblom et al., 1968, Montero et al., 2015a, Montero et al., 2015b).

Of note, Hill and colleagues (Hill et al., 1924, Hill and Lupton, 1923) used a discontinuous exercise protocol, with several bouts of progressively higher work rates to ascertain whether $\dot{V}O_{2max}$ was truly attained, whereas incremental exercise tests without breaks have now become the norm (Bentley et al., 2007b, Hawkins et al., 2007). In these tests, work rate increases over time either continuously (i.e. ramp exercise tests) or at regular intervals (i.e. graded exercise tests), until the tested individual reaches volitional exhaustion. Taylor (1941) was probably one of the first to adopt a continuous graded exercise test associated with measures of $\dot{V}O_2$. His studies established several cardiorespiratory and metabolic responses to a range of work rates, from light to severe, during exercise of constant or increasing intensity, often leading to the attainment of $\dot{V}O_{2max}$ and exhaustion (Taylor, 1941, Taylor, 1944). However, several important milestones regarding the $\dot{V}O_{2max}$ concept originated from studies using a discontinuous protocol (Mitchell et al., 1958, Taylor et al., 1955). For example, Taylor et al. (1955) were the first to establish objective criteria for the $\dot{V}O_{2max}$ plateau, and Mitchell et al. (1958) were the first to directly meausure the determinants of $\dot{V}O_{2max}$. It was much later, therefore, when the standardisation of ramp and graded exercise

tests became the focus of some investigations (Buchfuhrer et al., 1983, Froelicher Jr. et al., 1974, Whipp et al., 1981), that continuous protocols gained popularity.

2.2.2 – Fractional utilization of $\dot{V}O_{2max}$

Although successful endurance athletes typically possess a high $\dot{V}O_{2max}$ (Haugen et al., 2018, Saltin and Astrand, 1967), there may be very large differences in performance between trained individuals with similar $\dot{V}O_{2max}$ (Coyle et al., 1988, Sjödin and Svedenhag, 1985). This is because competitive performances are actually submaximal in several endurance events (Costill and Fox, 1969, Lucia et al., 2001). Exercise at $\dot{V}O_{2max}$ cannot be sustained for longer than a few minutes (Billat and Koralsztein, 1996), as the high-energy phosphate depletion and pH reduction that manifest during the highest intensities (Jones et al., 2008a, Vanhatalo et al., 2010) are associated with muscle fatigue (Fitts, 1994). Thus, endurance performance is also dependent on the fractional utilization of $\dot{V}O_{2max}$, which represents the highest metabolic rate that can be sustained for a given duration (Bassett Jr. and Howley, 2000, Coyle, 1995).

Costill and colleagues (Costill, 1970, Costill and Fox, 1969, Costill et al., 1973) were probably the first to investigate this matter. Initially, they identified an inverse relationship between competitive running distance and fractional utilization of $\dot{V}O_{2max}$, the latter being estimated based on athletes' personal best times and laboratory measures of $\dot{V}O_2$ at different speeds (Costill and Fox, 1969). Then, an inverse relationship between competitive running distance and $[La^-]$ at the end of the races was reported (Costill, 1970). Besides, an exponential relationship between $[La^-]$, following 5 min of running at selected speeds, and the $\%\dot{V}O_{2max}$ evoked was demonstrated (Costill, 1970). In a subsequent study, sixteen well-trained runners were split into four groups based on their best 16.1-km performance of the year (Costill et al., 1973). The fastest group exhibited the lowest $[La^-]$ for each running speed tested on a treadmill and also for each exercise intensity as $\%\dot{V}O_{2max}$ (Costill et al., 1973). Taken together, these studies showed that a) the longest the maximal exercise bout is, the lowest is the fractional utilization of $\dot{V}O_{2max}$ and $[La^-]$, and b) the exponential relationship between $[La^-]$ and running speed or $\%\dot{V}O_{2max}$ is right-shifted for the best athletes. These observations made it clear that the best athletes could perform exercise at selected work rates with lower $[La^-]$, allowing them to compete at higher $\%\dot{V}O_{2max}$. This conclusion was indeed confirmed by subsequent studies in which high correlations between endurance performance

and various thresholds of [La^-] were obtained (Coyle et al., 1988, Farrell et al., 1979, LaFontaine et al., 1981, Sjödin and Jacobs, 1981).

Today, there is a multitude of concepts to address the requirement for a single variable to inform the highest %$\dot{V}O_{2max}$ that can be sustained during endurance exercise (Faude et al., 2009, Jamnick et al., 2018, Meyer et al., 2005, Poole et al., 2021, Skinner and McLellan, 1980). The so-called blood lactate and ventilatory thresholds are believed to be linked by a common underlying mechanism, as the increased carbon dioxide output ($\dot{V}CO_2$) that characterises the ventilatory thresholds is associated with increased levels of exercise-induced metabolic acidosis (Jamnick et al., 2020, Meyer et al., 2005, Poole et al., 2021, Skinner and McLellan, 1980). While it is beyond the scope of this thesis to review this complex mechanism fraught with controversy (Hopker et al., 2011, Whipp and Ward, 2011), it must be acknowledged that these thresholds broadly reflect the oxidative capacity of the exercising muscles (Beever et al., 2020, Ivy et al., 1980, Poole et al., 2021). Endurance training leads to several adaptations at the muscle tissue level, such as increased capillarization (Andersen and Henriksson, 1977, Hoppeler et al., 1985, Ingjer, 1979) and mitochondrial content (Hoppeler et al., 1985, Ingjer, 1979, Montero and Lundby, 2017). With these structural changes, it becomes more difficult to stress muscle cells to their maximal respiratory capacity for adenosine triphosphate (ATP) resynthesis, ultimately causing less homeostatic disturbance (Egan and Zierath, 2013, Holloszy and Coyle, 1984), which is typically manifested as a lower [La^-] at the same work rate post- compared with pre-training (Ekblom et al., 1968, Hurley et al., 1984, Sjödin et al., 1982). In practical terms, these adaptations make it possible that individuals exercise at a higher %$\dot{V}O_{2max}$ in the trained state for a fixed time or distance, improving performance as a consequence.

2.2.3 – Efficiency/economy

Once it is understood that the highest the $\dot{V}O_{2max}$ and fractional utilization of $\dot{V}O_{2max}$ are, the greatest is the potential for distinguished endurance performance, it becomes natural to also conclude that exercising with a low submaximal $\dot{V}O_2$ is beneficial, as higher power outputs/speeds can be achieved for a given metabolic rate. In the context of cycling, efficiency represents the ratio between work and energy expenditure (Ettema and Lorås, 2009, Gaesser and Brooks, 1975, Hopker et al., 2009, Jobson et al., 2012). However, for other types of locomotion, work done cannot be easily quantified, and economy is the preferred measure, which is defined as the submaximal $\dot{V}O_2$ per unit of body mass elicited

during a given exercise task (Cavanagh and Kram, 1985, Daniels, 1985, Morgan et al., 1989). While efficiency is fairly constant among individuals (Ettema and Lorås, 2009, Hopker et al., 2009), economy varies substantially (Conley and Krahenbuhl, 1980, Costill et al., 1973, Farrell et al., 1979, Sjödin and Svedenhag, 1985). This is because speed reflects only part of the work done by the body, for example, in the case of running (Daniels, 1985), and differences in economy do not necessarily represent differences in efficiency (Cavanagh and Kram, 1985). In other words, to maintain a given speed, different athletes may need to exercise at different work rates, resulting in dissimilar metabolic rates. Nevertheless, there is direct evidence for the impact of either efficiency or economy upon endurance exercise performance (Conley and Krahenbuhl, 1980, Farrell et al., 1979, Horowitz et al., 1994, Jobson et al., 2012, Passfield and Doust, 2000, Sjödin and Svedenhag, 1985).

Research on efficiency/economy dates back to the 1920's (Dickinson, 1929, Hill et al., 1924, Hill and Lupton, 1923). However, still today, no true consensus as to the chief determinants of either efficiency or economy exists (Barnes and Kilding, 2015a, Hopker et al., 2009, Jobson et al., 2012, Morgan et al., 1989, Saunders et al., 2004). Often, the evidence is contradictory. One example is that the proportion of type I muscle fibres in the vastus lateralis has been shown to be positively associated (Horowitz et al., 1994) or not associated (Hopker et al., 2013) with cycling efficiency. Another example is that some authors have adopted a cautionary approach toward a general economical running technique (Moore, 2016, Williams and Cavanagh, 1987), whereas Folland et al. (2017) have even recommended specific stride parameters and lower limb angles to optimise running economy. As a matter of fact, a given efficiency/economy most likely results from a complex interplay between several metabolic, cardiorespiratory, biomechanical, and neuromuscular factors (Barnes and Kilding, 2015a, Hopker et al., 2009, Jobson et al., 2012, Saunders et al., 2004).

The trainability of efficiency/economy has also been a topic of debate (Barnes and Kilding, 2015b, Hopker et al., 2009, Jobson et al., 2012, Morgan et al., 1989). While it is generally acknowledged that some types of training such as HIIT can improve efficiency/economy (Barnes and Kilding, 2015b, Hopker et al., 2009, Jobson et al., 2012, Morgan et al., 1989), there are also studies suggesting otherwise (Daniels et al., 1978, Rønnestad et al., 2015, Skovereng et al., 2018, Smith et al., 2003). Given that the determinants of efficiency/economy are not totally understood (as mentioned above), it is unsurprising that

a consensus regarding the best training programmes to improve either variable is still lacking.

2.2.4 – Anaerobic capacity

In endurance disciplines that require drastic surges in exercise intensity, such as road cycling, mountain biking, or trail running (Abbiss et al., 2013, Born et al., 2017, Passfield et al., 2017, Stapelfeldt et al., 2004), a substantial proportion of the energetic demand is supplied via substrate-level phosphorylation as a rapid pathway for ATP resynthesis (Hargreaves and Spriet, 2018, Hultman and Greenhaff, 1991). This is because the responses of the cardiorespiratory and muscle bioenergetic systems lag behind any changes in work rate and cannot immediately accommodate an increased energetic demand (Rossiter, 2011). Accordingly, anaerobic capacity reflects the ability to produce maximal work at rates that cannot be met by oxidative phosphorylation (Green, 1994). Even though the kinetics of aerobic metabolism can be improved with training (Rossiter, 2011), ultimately, the reliance on anaerobic capacity cannot be avoided, particularly in competitive events where athletes typically produce a maximal end-spurt (Menaspà et al., 2015, Tucker et al., 2006, van Erp et al., 2021).

Early attempts to quantify the anaerobic component of exercise metabolism were made by Krogh and Lindhard (1920) and Hill and Lupton (1923). These authors recorded an approximately exponential increase and decrease of $\dot{V}O_2$ following the start and termination of exercise, respectively, at different work rates (Hill and Lupton, 1923, Krogh and Lindhard, 1913, Krogh and Lindhard, 1920). Krogh and Lindhard (1920) introduced the term "oxygen deficit" to reflect the time taken for $\dot{V}O_2$ to stabilise at the demand level, while Hill and Lupton (1923) introduced the term "oxygen debit" to reflect the time taken for $\dot{V}O_2$ to return to the pre-exercise level. It was believed that the oxygen deficit was compensated with anaerobic reactions of exergy transfer, whereas the oxygen debt was believed to be associated with the oxidation of anaerobic metabolism by-products (Hill and Lupton, 1923, Krogh and Lindhard, 1920). A decade later, the oxygen debt concept was modified to discriminate between an alactic and a lactic component (Margaria et al. 1933). However, in 1936, the oxygen debt phenomenon was shown to be independent of [La^-] (Bang, 1936), raising questions over the accepted theory at the time. Yet, this concept somehow evolved and prevailed as the maximal accumulated oxygen deficit, suggested by Medbø et al. (1988) to represent anaerobic capacity.

The maximal accumulated oxygen deficit is calculated from the relationship between work rate and $\dot{V}O_2$, whereby extrapolation provides an estimate of the $\dot{V}O_2$ demand associated with a certain work rate that leads to exhaustion in between 2 and 3 min (Medbø et al., 1988, Noordhof et al., 2013). The actual total $\dot{V}O_2$ (i.e. accumulated) is then subtracted from the estimated total $\dot{V}O_2$ (Medbø et al., 1988, Noordhof et al., 2013). While the maximal accumulated oxygen deficit is probably the most common estimate of anaerobic capacity today (Noordhof et al., 2013), there remain questions regarding its methodology and validity (Bangsbo, 1996, Noordhof et al., 2010). This might explain why anaerobic capacity has been so little explored from an endurance performance point of view compared with $\dot{V}O_{2max}$, fractional utilization of $\dot{V}O_{2max}$, and efficiency/economy (Joyner and Coyle, 2008). Indeed, some descriptions of the cardiovascular/anaerobic model presented here do not even mention it (Bassett Jr. and Howley, 2000, Coyle, 1995).

2.2.5 – Interaction of performance determinants

Endurance exercise performance is a multifaceted concept that results from the interaction of four main physiological determinants: $\dot{V}O_{2max}$, lactate/ventilatory threshold as an index of the fractional utilization of $\dot{V}O_{2max}$, efficiency/economy, and anaerobic capacity. It is interesting to note, however, that this interaction does not seem to be "static". Changing one component of performance is likely to affect the others (Hopker et al., 2012, Lucía et al., 2002, Skovereng et al., 2018). This poses a challenge for practitioners and scientists involved in the design of training programmes, and also suggests that performance should be assessed alongside physiological measures to monitor the effectiveness of a given intervention.

2.3 – Training regulation

Training consists of systematic and repeated exercise sessions performed by individuals/athletes with the goal of eliciting chronic physiological adaptations that allow for an increased exercise capacity/performance (Mujika, 2017). Training regulation thus refers to a set of decisions on how exercise sessions should be performed (mode, frequency, duration, and intensity) and organised over time. It is generally accepted that exposure to training leads to enhanced physiological function through gradual changes in the protein content and enzymatic activity of the cells of various tissues, secondary to the activation and/or repression of signalling pathways that govern gene expression (Egan and Zierath, 2013, Flück, 2006, Hawley et al., 2014, Perry et al., 2010). In other words, the chronic

adaptations to training reflect the cumulative effect of acute responses to exercise (Figure 2.3).

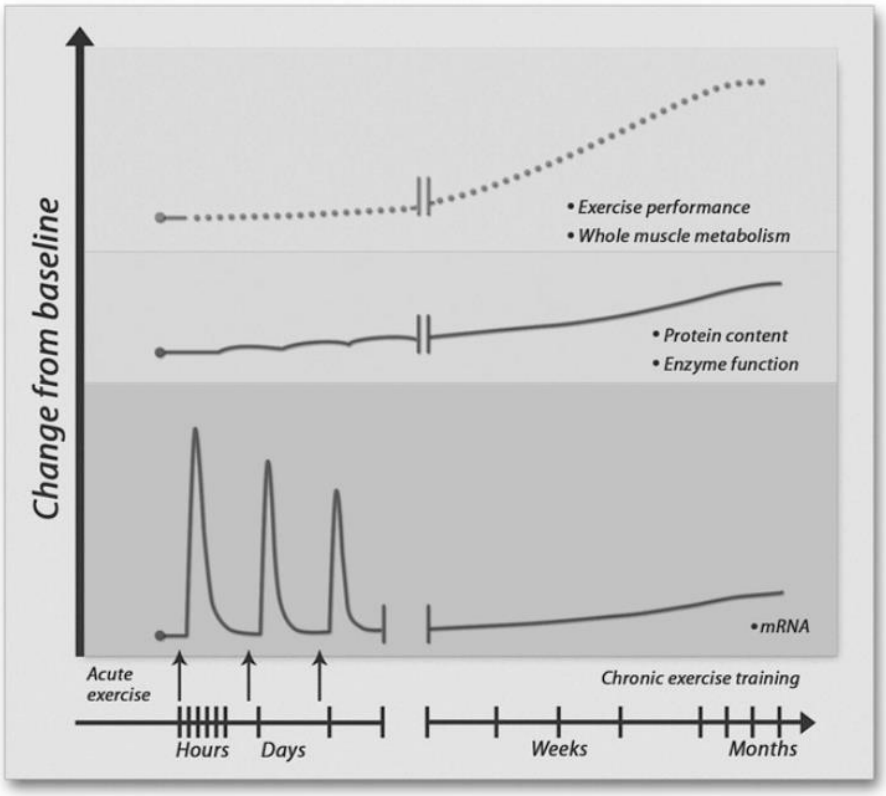

Figure 2.3 – Schematic representation of the molecular basis of adaptations to a training programme. Taken from Egan and Zierath (2013) p. 163.

Whether individual exercise sessions stress the organism enough to kickstart an adaptive process depends on the baseline status of an individual and the training dose (Hickson et al., 1981, Manzi et al., 2009a, Perry et al., 2010, Phillips et al., 1996); with training dose defined here as the product of mode, frequency, duration, and intensity of exercise sessions (Howley, 2001). Hickson and colleagues (Hickson et al., 1977, Hickson et al., 1981) conducted studies that demonstrate well this phenomenon. In one study, nine individuals were submitted to a training programme involving 40-min sessions, six days per week, with target work rates being adjusted to a higher level only once, at week 5 (Hickson et al., 1981). For the first three weeks, $\dot{V}O_{2max}$ increased, but remained constant afterwards. Post work rate adjustment, $\dot{V}O_{2max}$ again increased for the first three weeks only. A similar pattern was also observed for heart rate (HR) and [La^-] responses to the same work rates, where training led to diminishing returns as individuals adapted (Hickson et al., 1981). However, in another study

involving a similar training programme, but with weekly increases in work rate (Hickson et al., 1977), $\dot{V}O_{2max}$ rose continuously for the duration of the study (see Figure 1.1 above). Together, these two studies suggest that training needs to be manipulated once the organism becomes accustomed to the prescribed dose. In the next sections, it will be demonstrated how each component of training prescription affects the training dose and consequently the potential for adaptive responses.

One important caveat for the interpretation of the literature on training regulation is that performance and physiological adaptations to a training intervention are often dissociated (Daniels et al., 1978, Inglis et al., 2019, Ramsbottom et al., 1989, Vollaard et al., 2009). Yet, many training studies have only included $\dot{V}O_{2max}$ as a dependent variable (Pollock, 1973, Tanaka, 1994, Wenger and Bell, 1986), which may contribute to a biased overall picture of how training should be programmed. Indeed, just recently, the first meta-analyses were published with HIIT guidelines to optimise performance (Rosenblat et al., 2021, Rosenblat et al., 2020), suggesting that researchers are at least starting to address this problem.

2.3.1 – Mode

For the purposes of this literature review, mode refers to the type of locomotion chosen for exercise training. In some contexts, mode may also refer to how an exercise session is organised, as either continuous or intermittent training. This latter aspect of training will be referred to as pattern, being separately reviewed in Section 2.3.5 – Intermittent versus continuous exercise.

Cycling and running are likely the most practised endurance sports (Ham et al., 2009, Stamatakis and Chaudhury, 2008). Due to the simplicity with which exercise intensity can be controlled and manipulated in the laboratory, by changing power output of a cycle ergometer and speed or gradient of a treadmill, these exercise modes have also been the preferred choices of researchers. Cyclists and runners thus benefit from an extensive literature to inform training (Barnes and Kilding, 2015b, Billat, 2001, Hopker et al., 2009, Laursen and Jenkins, 2002, Lucia et al., 2001, Midgley et al., 2006, Passfield et al., 2017, Seiler and Tønnessen, 2009). In contrast, swimmers, rowers, and cross-country skiers, to name athletes of a few other disciplines, often rely on the generalisability of non-specific knowledge. As the cardiorespiratory system overload largely depends on the active muscle mass (Lewis et al., 1983, Stamford et al., 1978, Zhang et al., 2021), chronic responses to a

training programme are broadly considered mode-independent, at least for central adaptations (Pollock, 1973, Tanaka, 1994). However, when it comes to peripheral adaptions, the specificity principle applies. Most training-induced adaptations only occur in the muscle fibres recruited during exercise, with little (if any) adaptive response manifesting in the untrained musculature (McCafferty and Horvath, 1977, Reilly et al., 2009, Tanaka, 1994). These observations suggest that a) transferring the findings of cycling and running studies to other modes of locomotion requires careful evaluation, and b) the training dose interacts with exercise mode. How this interaction occurs has been a matter of debate for decades (Reilly et al., 2009, Tanaka, 1994), and it is currently unclear the extent to which mixing different exercise modes as part of a training program is beneficial/harmful. While it is generally acknowledged that mode-specific adaptations are suboptimal for multiple compared with single exercise modes when the amount and intensity of training are controlled for (Reilly et al., 2009, Tanaka, 1994), the largest $\dot{V}O_{2max}$ gain ever reported (1.19 $L \cdot min^{-1}$ or 39%) resulted from a 10-week training programme that involved cycling and running on alternate days (Hickson et al., 1977). The fact that participants were untrained at the beginning of the training programme likely contributed to this remarkable improvement. However, there was no evidence that $\dot{V}O_{2max}$ gains diminished towards the end of the programme when participants were much fitter (Hickson et al., 1977). Contradictions aside, until future research elucidates the circumstances determining the success of combined-mode training interventions, the investigation/interpretation of training frequency, duration, and intensity should be restricted to single-mode training studies.

2.3.2 – Frequency

Training frequency represents how often training sessions are repeated. There are three main approaches to investigate the effect of training frequency on adaptive responses. In the first approach, the length of the training programme in weeks is held constant, whereas frequency determines the overall training dose (i.e. the more training sessions are performed per week, the higher the dose is). In the second approach, the total number of sessions is held constant, whereas frequency determines the length of the training programme. In the third approach, both the training programme length and the exercise dose are held constant, whereas exercise duration is manipulated (e.g. two 30-min sessions per day versus a single 60-min session per day). For the purposes of this review, training frequency will be considered in the sense that it directly affects the exercise dose (i.e. first approach). While the impact of frequency (in all its forms) on adaptive responses to training has yet to be fully elucidated, the first

approach has been the focus of most studies (Garber et al., 2011, Montero and Lundby, 2017, Nordesjö, 1974, Pollock, 1973, Wenger and Bell, 1986).

It is generally acknowledged that the higher the training frequency is (within certain limits), the greater is the potential for training adaptations (Garber et al., 2011, Montero and Lundby, 2017, Nordesjö, 1974, Pollock, 1973, Wenger and Bell, 1986). It is therefore not surprising that competitive endurance athletes train pretty much daily, and sometimes more than once per day (Billat et al., 2001, Billat et al., 1999b, Costill et al., 1991, Seiler and Kjerland, 2006, van Erp et al., 2019). However, it is also clear that training frequency interacts with intensity and duration (Garber et al., 2011, Wenger and Bell, 1986). Depending on the combination of these variables, training may become excessive, leading to chronic fatigue and maladaptation (Billat et al., 1999b, Foster, 1998, Kenttä and Hassmén, 1998). For example, it has been suggested that high-intensity sessions can be performed up to five times a week, although the recommended optimal frequency varies markedly between studies (Billat et al., 1999b, Foster, 1998, Garber et al., 2011, Rosenblat et al., 2021, Seiler and Tønnessen, 2009, Wenger and Bell, 1986). This is likely due to the difficulty in isolating frequency from the other components of training dose, which complicates the interpretation of the literature.

From a practical perspective, a high frequency of exhaustive training sessions may also be difficult to accomplish. In a study wherein high-intensity sessions were performed six times per week, participants refused to continue the training programme after the pre-planned 10 weeks "for the reason that they found exercise of this frequency and intensity too tiring and time-consuming" (Hickson et al., 1977). Although this programme was very effective in increasing $\dot{V}O_{2max}$ (Hickson et al., 1977), participants' anecdote suggests adherence must be considered in a long-term approach to training regulation, which might influence the optimal combination of training frequency and intensity, and duration.

2.3.3 – Duration

Duration refers to the length in time of a given exercise training session. If duration is compounded (e.g. total exercise duration per week), it is usually referred to as volume. There is some evidence that as exercise durations increase, so does the potential for training adaptations (Bishop et al., 2019, Garber et al., 2011, Nordesjö, 1974, Pollock, 1973, Seiler and Tønnessen, 2009, Wenger and Bell, 1986). However, there seems to be a limit, as at some point competitive endurance athletes that often exercise for three or more hours per

day (Billat et al., 2001, Costill et al., 1991, van Erp et al., 2019) do not seem to benefit from extra training volume (Costill et al., 1991, Laursen and Jenkins, 2002, Sjödin and Svedenhag, 1985). While thirty to sixty minutes of daily exercise are recommended for untrained individuals (Garber et al., 2011), the optimal training duration has yet to be established for athletes of different fitness levels.

The prescription of exercise duration should be considered together with intensity, as the effect of these variables on adaptive responses to training interacts largely (Garber et al., 2011, MacInnis and Gibala, 2017, Seiler et al., 2013, Wenger and Bell, 1986). Human performance is characterised by a curvilinear relationship (Figure 2.4) wherein the higher the exercise intensity is, the progressively shorter is the duration with which exercise can be sustained (García-Manso et al., 2012, Hill, 1925, Nikolaidis et al., 2017). This suggests that for small reductions in exercise intensity, training duration needs to increase considerably to challenge the organism to the same extent (Hofmann and Tschakert, 2017, Nordesjö, 1974). It is therefore not surprising that relatively few studies have documented the relationship between training duration and adaptive responses to training (Bishop et al., 2019, Laursen, 2010, Nordesjö, 1974, Pollock, 1973, Wenger and Bell, 1986), as this type of investigation may require impractically long exercise sessions if training is to be conducted at the moderate-intensity range.

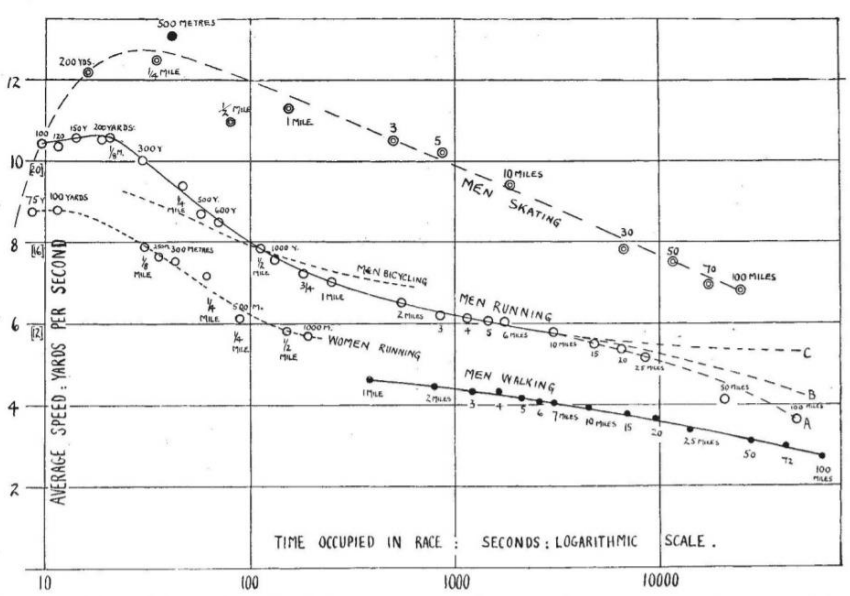

Figure 2.4 – The relationship between average speed (y-axis) and racing time (x-axis; logarithmic scale) of world records for skating, bicycling, running, and walking. Taken from Hill (1925) p. 547.

2.3.4 – Intensity

Intensity refers to the overload of the cardiorespiratory and musculoskeletal systems, which is dependent on the work rate during exercise. It may be expressed in absolute terms (e.g. 200 W for cycling or 11 $km \cdot h^{-1}$ for running, eliciting a $\dot{V}O_2$ of 2.8 $L \cdot min^{-1}$), or in relative terms (60%$\dot{V}O_{2max}$ for an individual with a $\dot{V}O_{2max}$ of 4.7 $L \cdot min^{-1}$). In the context of a group, the prescription of exercise intensity in absolute terms is not recommended because a given work rate may elicit various levels of cardiorespiratory and metabolic stress according with each individual's physiological capacity (Garber et al., 2011, Howley, 2001). For this reason, training intensity has been commonly referred to in relative terms.

Within the range of approximately 50% to 100%$\dot{V}O_{2max}$, there is a general positive relationship between training intensity and the potential for adaptive responses (Figure 2.5) (Garber et al., 2011, MacInnis and Gibala, 2017, Nordesjö, 1974, Pollock, 1973, Wenger and Bell, 1986), although this is not an undisputed finding (Scribbans et al., 2016). The reason for this discrepancy likely resides in the fact that long training sessions might compensate for a low training intensity, at least in the case of untrained individuals (Bishop et al., 2019, Garber et al., 2011, Milanovic et al., 2015, Nordesjö, 1974, Pollock, 1973, Scribbans et al., 2016, Wenger and Bell, 1986). However, when it comes to endurance-trained athletes that already train for long hours, mostly at low intensity (Billat et al., 2001, Seiler and Kjerland, 2006, van Erp et al., 2019), the picture is slightly different. It has been suggested that frequently training at or near $\dot{V}O_{2max}$ may be required to potentiate the adaptive response (Buchheit and Laursen, 2013, Laursen, 2010, Laursen and Jenkins, 2002, Londeree, 1997, Midgley and McNaughton, 2006, Midgley et al., 2006, Seiler and Tønnessen, 2009).

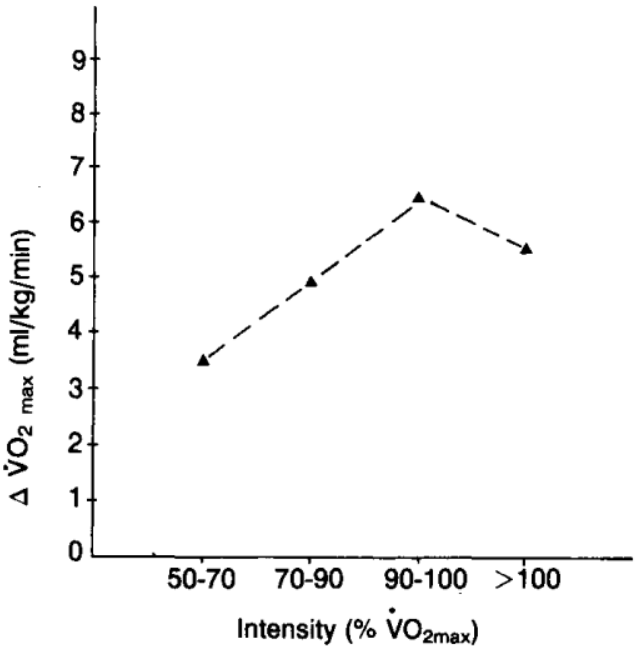

Figure 2.5 – The relationship between adaptive $\dot{V}O_{2max}$ responses (y-axis) and the intensity of training (x-axis) irrespective of frequency, duration, training programme length, and initial fitness level. Taken from Wenger and Bell (1986) p. 347.

Exercising at or near $\dot{V}O_{2max}$ is not without its challenges though. These intensities are associated with rapid exhaustion, limiting the duration with which exercise can be sustained (Billat and Koralsztein, 1996, Draper et al., 2003, Hill et al., 2002). Accordingly, intermittent training sessions have been the preferred choice of athletes and non-athletes seeking to maximise the training duration at work rates associated with the highest $\%\dot{V}O_{2max}$ (Billat et al., 2000, Christensen et al., 1960, Midgley and McNaughton, 2006). Given that intermittent exercise can be configured in multiple ways (Billat, 2001, Buchheit and Laursen, 2013, Tschakert and Hofmann, 2013), the interaction between exercise intensity and duration on adaptive responses to training (see Section 2.3.3 – Duration) becomes more complicated, as the pattern of work rate changes may contribute to the magnitude of training adaptations (Bacon et al., 2013, Rosenblat et al., 2021, Seiler et al., 2013, Wen et al., 2019). This aspect of training regulation is reviewed next, in Section 2.3.5 – Intermittent versus continuous exercise.

2.3.5 – Intermittent versus continuous exercise

Intermittent exercise refers to systematic changes in work rate during a training session to establish bouts of contrasting intensity (i.e. work and recovery intervals) (Figure 2.6).

Usually, intermittent exercise is performed as HIIT, in which the work intervals are performed within the very heavy intensity domain, with $\dot{V}O_2$ progressively increasing, while recovery intervals are performed within the moderate intensity domain (some regimes use rest), with $\dot{V}O_2$ progressively decreasing, although the exact $\dot{V}O_2$ kinetics is largely determined by the duration of each bout (Figure 2.7; see Rossiter (2011) for full explanation and definition of intensity domains).

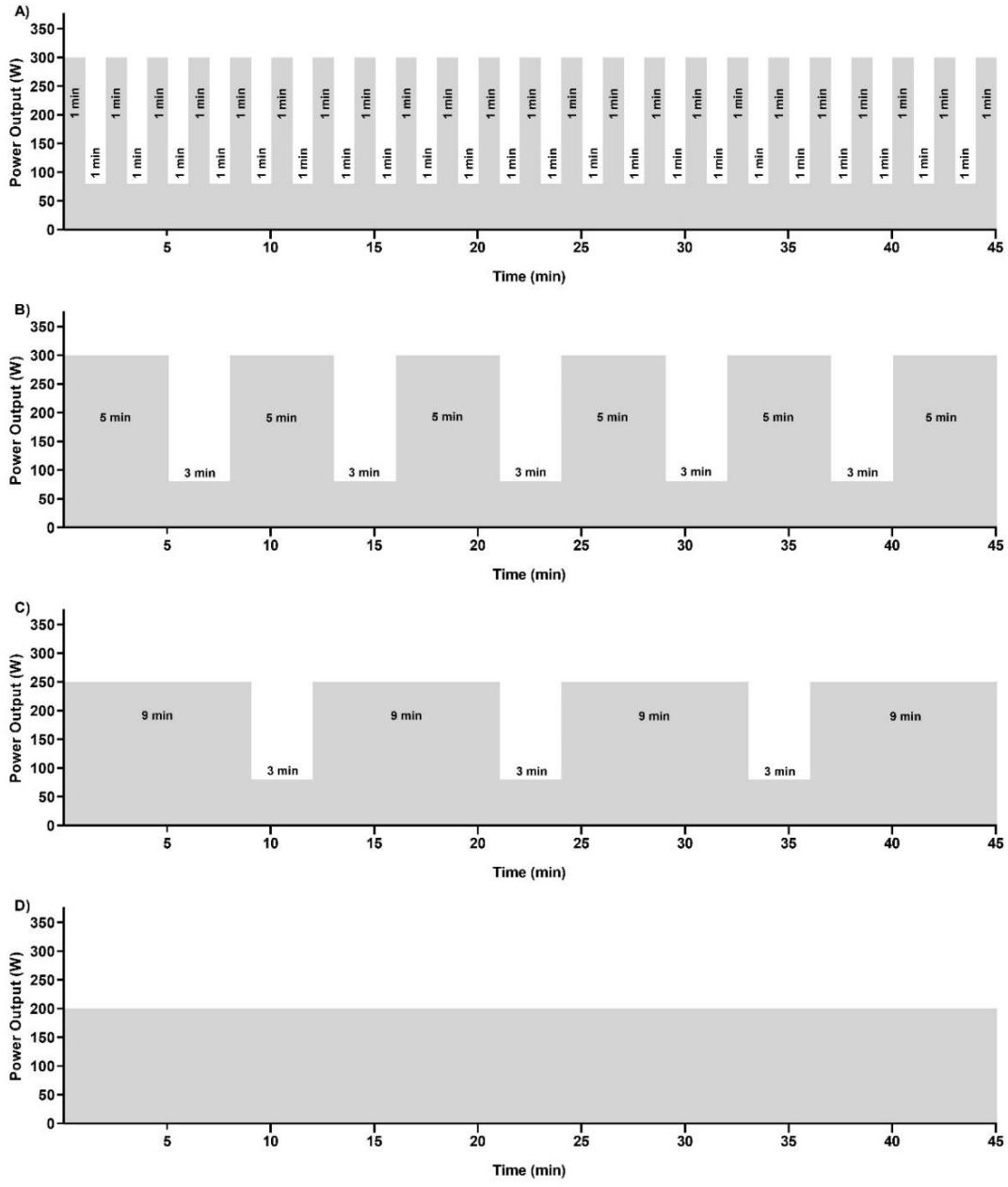

Figure 2.6 – Schematic representation of some different patterns with which intermittent exercise can be configured (panels A, B, and C) and continuous exercise (panel D).

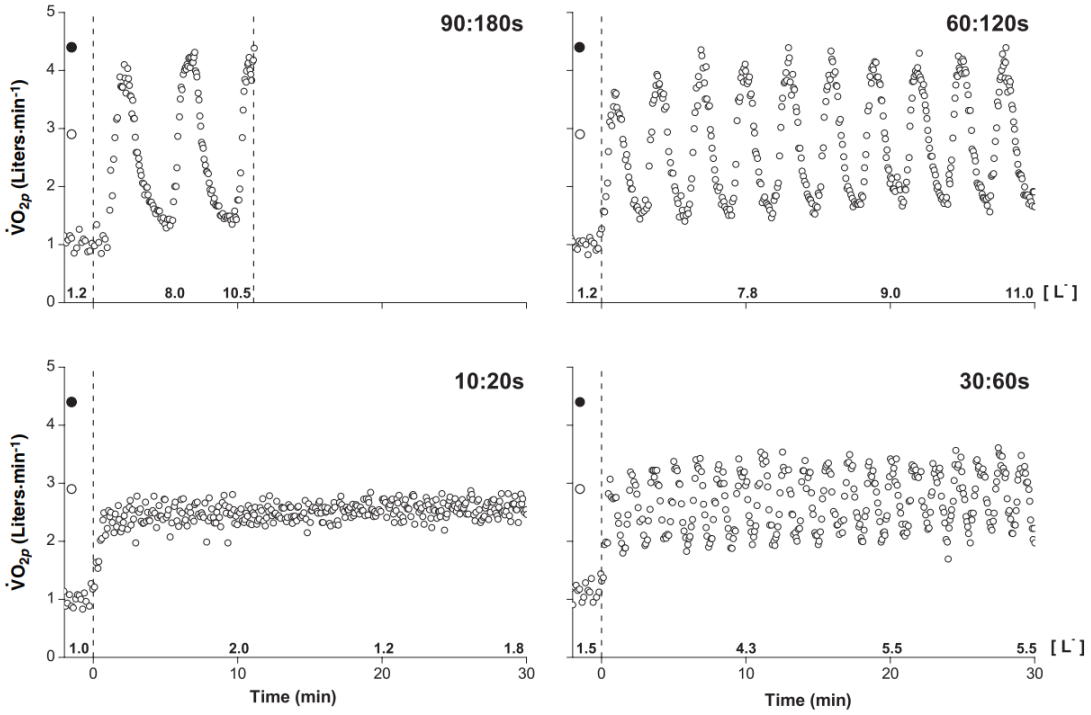

Figure 2.7 – Pulmonary oxygen uptake responses to ($\dot{V}O_{2p}$) to high-intensity interval training sessions performed at the same exercise intensities but different work and recovery interval durations (inset to each panel, at the top right). Solitary solid and open circles along the y-axis represent the $\dot{V}O_{2p}$ associated with maximal oxygen uptake and gas exchange threshold. Taken from Rossiter (2011) p. 219.

The first studies on intermittent exercise were performed at the turn of the 1950's, in which the effect of different work/recovery interval durations was investigated at a given work rate (Åstrand et al., 1960a, Åstrand et al., 1960b, Christensen, 1960, Christensen et al., 1960, Reindell and Roskamm, 1959). By using a Fleisch metabograph (i.e. closed-circuit apparatus, see Montani et al. (2018) for details), Reindell and Roskamm (1959) established that $\dot{V}O_2$ was higher during the recovery intervals compared with the work intervals, leading authors to conclude that the recovery intervals played the chief role in determining the magnitude of physiological overload during high-intensity intermittent cycling. That conclusion was challenged by Christensen (1960), who used Douglas bags (i.e. open-circuit apparatus) to record the highest $\dot{V}O_2$ always during the work intervals, irrespective of the session format. Christensen (1960) concluded that it was actually the duration of the work intervals that mattered the most, and he attributed the higher $\dot{V}O_2$ during the recovery intervals to a delayed response of the metabograph employed by Reindell and Roskamm

(1959). The rebuttal of Christensen (1960) built on previous, also cycling-based investigations with work and recovery intervals of identical (from 30 s to 3 min) (Åstrand et al., 1960a) and dissimilar durations (work and recovery intervals varying from 10 to 60 s and from 20 s to 4 min, respectively) (Åstrand et al., 1960b). Subsequently, in a more thorough investigation comparing intermittent versus continuous running at high intensity, it was confirmed that the length of work intervals greatly affects the magnitude of cardiorespiratory and metabolic responses (Christensen et al., 1960), which is consistent with the current understanding (Billat, 2001, Buchheit and Laursen, 2013, Davies et al., 2017, Midgley and McNaughton, 2006, Rossiter, 2011).

Another important contribution of the seminal studies on intermittent exercise was the demonstration that both the musculoskeletal and cardiorespiratory systems can be stressed without major engagement of the glycolytic metabolism, as inferred by a low [La^-], during intermittent training with short (≤ 30 s) work and recovery intervals (Åstrand et al., 1960a, Åstrand et al., 1960b, Christensen et al., 1960). Accordingly, with different combinations of work/recovery interval intensity and duration, it may be possible to selectively train a particular component of physical fitness (Billat, 2001, Buchheit and Laursen, 2013, Midgley and McNaughton, 2006, Tschakert and Hofmann, 2013). However, it is important to emphasise that adaptive responses to training are complex and may not purely reflect the intended stimulus (Mann et al., 2014, Meyler et al., 2021), particularly in the context of intermittent exercise. The relative contribution of phosphocreatine hydrolysis, glycolysis, and oxidative phosphorylation to ATP turnover during intermittent exercise may shift dramatically from the beginning to the end of intermittent exercise sessions (Gaitanos et al., 1993, Parolin et al., 1999, Spriet et al., 1989), which is obviously difficult to account for.

Intermittent exercise is also peculiar in the sense that interactions between the prescription elements of work intervals may play a major role in the adaptive responses to training (Bacon et al., 2013, Rosenblat et al., 2021, Rosenblat et al., 2020, Seiler et al., 2013, Wen et al., 2019), although studies are often controversial in this respect. For example, Åstrand et al. (1960a) predicted that HIIT with 3-min work and recovery intervals would produce a great adaptive response upon the cardiorespiratory system, with some meta-analyses later confirming that the largest $\dot{V}O_{2max}$ and performance gains are associated with long work intervals (Bacon et al., 2013, Rosenblat et al., 2021, Rosenblat et al., 2020, Wen et al., 2019). However, when cyclists perform short work intervals at a higher intensity than would be

otherwise possible for long work intervals, they seem to benefit more (Rønnestad et al., 2020, Rønnestad et al., 2015, Turnes et al., 2016). While these contrasting results may reflect fitness level differences between samples, it is also conceivable that meta-analytical effects overlook the minutiae of intermittent exercise prescription, suggesting that more studies are warranted to enable reliable conclusions.

While intermittent exercise training has often been associated with adaptive responses of the largest magnitudes (Bacon et al., 2013, MacInnis and Gibala, 2017, Milanovic et al., 2015, Wen et al., 2019, Wenger and Bell, 1986), it is also true that comparisons against continuous exercise are often made by matching total work (MacInnis and Gibala, 2017, Maturana et al., 2021), which may artificially constrain the intensity of continuous training and cause large imbalances in terms of cardiorespiratory and metabolic overload, as well as post-exercise fatigue (Kesisoglou et al., 2021, Kesisoglou et al., 2020). In other words, the comparison of intermittent versus continuous exercise ends up being biased by the confounding effect of intensity. Accordingly, it has been argued that continuous and intermittent exercise should be matched on the basis of the maximal sustainable work rate of each session, the so-called isoeffort approach (Nicolò et al., 2014, Nicolò and Girardi, 2016). Notwithstanding the fact that the isoeffort approach has seldom been adopted in training studies for comparisons between intermittent and continuous exercise (see Henriksson and Reitman (1976) for exception), it has been proposed that the regular alternation in work rate plays a role in evoking adaptive responses independently of intensity and duration with which work and recovery intervals are performed (Jiménez-Pavón and Lavie, 2017). This hypothesis finds some support in the evidence that intermittent submaximal exercise elicits greater activation of signalling pathways associated with mitochondrial biogenesis compared with continuous exercise of similar total work and intensity (Combes et al., 2015, Popov et al., 2014). However, there is also evidence to the contrary for maximal exercise (Cochran et al., 2014, Taylor et al., 2016), indicating that this aspect of training regulation is yet to be fully elucidated. The fact that molecular biomarkers of adaptive potential are subject to a large random error and/or biological variability (Islam et al., 2021, Islam et al., 2019) complicates further the interpretation of acute studies diverging in their findings (Cochran et al., 2014, Combes et al., 2015, Popov et al., 2014, Taylor et al., 2016). Overall, it is likely that intermittent exercise is neither better nor worse than continuous. Rather, the exercise pattern brings an element of specificity to the regulation of training, which manifests as chronic adaptations that are unique to either

intermittent or continuous training programmes (Cochran et al., 2014, Gorostiaga et al., 1991, Henriksson and Reitman, 1976).

2.3.6 – Does one size fit all?

For the non-specialist, getting a solid grasp of the endurance training literature may be difficult, due to the infinitude of training studies published since the pioneering attempts of Robinson and Harmon (1941) and Knehr et al. (1942). As a matter of fact, the present literature review has often relied on the conclusions of several previous reviews to synthesise knowledge and identify consensus/discord. Despite the large number of studies, it is only possible to pick out general trends when it comes to the design of optimal training regimes, as, in practice, rather contrasting approaches may prove effective (e.g. Stepto et al. (1999)). This leaves practitioners free to use their creativity when implementing exercise interventions to best accommodate the needs of an individual or group. On the other hand, resources may be wasted when gains in performance and physiological function do not live up to the expectations.

2.4 – Variability in training adaptation

Variability in training adaptation refers to the differences in magnitude to which different individuals respond to a common training programme (inter-individual variability), or the differences in magnitude to which an individual responds to the same training programme when repeated on distinct occasions (intra-individual variability). For the purposes of this literature review, inter-individual variability will be the focus, although intra-individual variability will be mentioned as appropriate.

While the inter-individual variability of many adaptive responses to endurance training has been investigated (Bouchard, 1983, Bouchard and Rankinen, 2001, Corbett et al., 2018, Mann et al., 2014, Nummela et al., 2021, Vollaard et al., 2009), including performance itself (Astorino et al., 2018, Coakley and Passfield, 2018b, Lortie et al., 1984, Vollaard et al., 2009), the literature on $\dot{V}O_{2max}$ is far more comprehensive (Bouchard et al., 1999, Hecksteden et al., 2018b, Meyler et al., 2021, Ross et al., 2019, Williams et al., 2019, Williamson et al., 2017). Thus, the variability in $\dot{V}O_{2max}$ adaptative responses to training will predominate in this and the sections that follow. As with the literature on training regulation (see Section 2.3 – Training regulation), caution should be exercised when generalising

findings based on $\dot{V}O_{2max}$ only, as conclusions may not necessarily hold for other physiological indexes and performance.

The first studies on the concept of inter-individual variability in adaptive responses to endurance training were published in the 1980's (Bouchard, 1983, Boulay et al., 1986, Hamel et al., 1986, Lortie et al., 1984, Prud'homme et al., 1984, Simoneau et al., 1986). At that time, there was a strong interest in the genetic determinants of the magnitude of adaptive responses (Bouchard et al., 1988, Bouchard and Lortie, 1984). Years later, a large multi-centre study was devised by Bouchard et al. (1995) to investigate the role of genetics in the adaptations to a 20-week training programme comprising 60 sessions of cycling that progressed from 30 to 50 min in duration, and from 55% to 75%$\dot{V}O_{2max}$ in intensity (i.e. the HERITAGE family study). With hundreds of participants taking part, the magnitude of inter-individual variability in $\dot{V}O_{2max}$ gains was substantial, ranging from < 0 to > 1000 ml·min^{-1} (Figure 2.8) (Bouchard et al., 1999, Bouchard and Rankinen, 2001), despite the HERITAGE family study being described as a rigorous intervention, with well-controlled and carefully chosen protocols (Gagnon et al., 1996). Adaptive variability following standardised training has since been assumed a ubiquitous phenomenon, although not without controversy (Atkinson and Batterham, 2015, Bonafiglia et al., 2019a, Hecksteden et al., 2018b, Joyner and Lundby, 2018, Shephard et al., 2004, Williamson et al., 2017), with the publications of Bouchard and colleagues (Bouchard et al., 1999, Bouchard and Rankinen, 2001, Bouchard et al., 2011, Skinner et al., 2001) setting a strong foundation for the current literature on determinants of $\dot{V}O_{2max}$ response to endurance training (Mann et al., 2014, Meyler et al., 2021, Sarzynski et al., 2017). These determinants will be reviewed in the next sections.

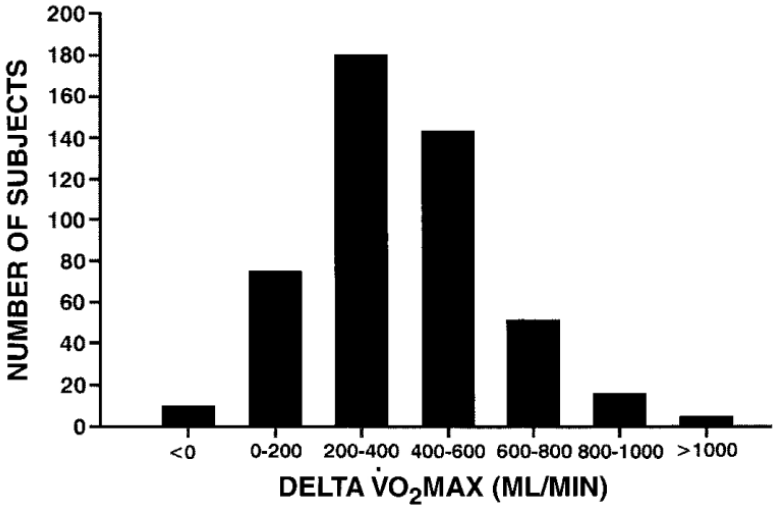

Figure 2.8 – Histogram of $\dot{V}O_{2max}$ responses to 20 weeks of endurance training. Data from 481 participants of the HERITAGE family study (Bouchard et al., 1999). Taken from Bouchard et al. (1999) p. 1005.

2.4.1 – Genetics and training adaptation

The existence of large inter-individual differences in $\dot{V}O_{2max}$ among either untrained individuals (Bouchard et al., 1998, Kaminsky et al., 2015, Loe et al., 2013) or endurance athletes (Haugen et al., 2018, Saltin and Astrand, 1967) is a well-established fact. Intuitively, one can attribute these differences to genetic influences. However, the reality is likely more complex as even researchers do not seem to agree on the robustness of the evidence for the role of genetics in the fitness variability observed in humans (Bouchard, 2019, Joyner, 2019). Besides, epigenetics may also play a role in the determination of athletic potential, complicating the interpretation of (purely) genetics studies (Denham et al., 2014, Ehlert et al., 2013).

Drawing upon the principles of genetic family studies (Fisher, 1919), Klissouras (1971) was likely the first to investigate the extent to which genetic predisposition accounts for the inter-individual variability in $\dot{V}O_{2max}$ ($ml \cdot kg^{-1} \cdot min^{-1}$). Boys, rather than adults, were recruited to minimise the effect of environmental differences on the observed phenotype. With a sample of fifteen monozygotic (i.e. identical genetic makeup) and ten dizygotic twins (i.e. approximately 50% of genes are shared), a heritability estimate of 93% was established. Besides, the intra-pair correlation for $\dot{V}O_{2max}$ reached 0.91 for monozygotic, but only 0.44 for dizygotic twins (Klissouras, 1971). In a subsequent study, in which Klissouras et al. (1973) included adults as part of a sample of twenty-three monozygotic and sixteen dizygotic

twins, intra-pair differences were significant only for the latter group. This study thus corroborated previous findings despite not controlling for environmental influences, reflecting the strength of the genetic basis of $\dot{V}O_{2max}$.

Later twin (Bouchard et al., 1986, Fagard et al., 1991, Sundet et al., 1994) and family studies (Bouchard et al., 1998, Lesage et al., 1985, Montoye and Gayle, 1978) produced rather distinct heritability estimates and did not always support the figure introduced by Klissouras (1971). For instance, Bouchard et al. (1998) investigated members of eighty-six nuclear families, all sedentary, and reported that there was up to 2.9 higher variability in $\dot{V}O_{2max}$ between than within families. However, Bouchard et al. (1998) estimated a maximal $\dot{V}O_{2max}$ ($ml \cdot min^{-1}$) heritability of approximately 50% by adjusting for age, sex, and body mass. While estimates of Bouchard et al. (1998) are much more conservative than those reported by Klissouras (1971), a meta-analysis that incorporated these and other studies, as well as authors' own dataset, arrived at figures of 59% ($ml \cdot min^{-1}$) and 72% ($ml \cdot kg^{-1} \cdot min^{-1}$) (Schutte et al., 2016). These numbers are somewhat similar to those reported by Miyamoto-Mikami et al. (2018), who conducted a systematic review and meta-analysis and arrived at 68% ($ml \cdot min^{-1}$) and 56% ($ml \cdot kg^{-1} \cdot min^{-1}$). Taken together, twin and family studies suggest that genetics accounts for more than 50% of the inter-individual variability in $\dot{V}O_{2max}$, although the 93% figure of the seminal study by Klissouras (1971) is likely to have been substantially overestimated.

The aforementioned heritability studies are all cross-sectional, meaning that they cannot inform how genetic predisposition accounts for the inter-individual variability in $\dot{V}O_{2max}$ changes resulting from a training programme. It may be argued that how an individual adapts to a training programme is more relevant than his/her baseline fitness level. After all, a large trainability can compensate for relatively low levels of initial fitness. Accordingly, twin (Boulay et al., 1986, Hamel et al., 1986, Prud'homme et al., 1984) and family studies (Bouchard et al., 1999, Bouchard et al., 2011, Gaskill et al., 2001a, Pérusse et al., 2001) have also been employed to interrogate the genetic basis of adaptive responses to endurance training programmes.

In studies with only monozygotic twins, such as those conducted by Boulay et al. (1986), Hamel et al. (1986), and Prud'homme et al. (1984), it is common to quantify the intraclass correlation coefficient (ICC) as a measure of intra-twin resemblance as a function of the total

variability of the sample. The higher the ICC is, the higher the genetic component of a given adaptive response is. What the twin studies suggest is that changes in a 90-min time-trial performance ($kJ \cdot kg^{-1}$) following training may be more genetically determined than changes in $\dot{V}O_{2max}$ ($ml \cdot kg^{-1} \cdot min^{-1}$), GET ($ml \cdot kg^{-1} \cdot min^{-1}$), or RCP ($ml \cdot kg^{-1} \cdot min^{-1}$) (Boulay et al., 1986, Hamel et al., 1986, Prud'homme et al., 1984). In these studies, ICC ranged from 0.69 to 0.81 for the time-trial performance (Boulay et al., 1986, Hamel et al., 1986), from 0.44 to 0.74 for $\dot{V}O_{2max}$ (Boulay et al., 1986, Hamel et al., 1986, Prud'homme et al., 1984), and from close to 0 (i.e. minimal genetic influence) to 0.43 for GET and RCP (Boulay et al., 1986, Prud'homme et al., 1984).

Family studies also suggest that the genetic component of adaptive responses to training is stronger for $\dot{V}O_{2max}$ ($ml \cdot min^{-1}$) compared with submaximal exercise parameters, such as GET ($ml \cdot min^{-1}$) and the $\dot{V}O_2$ or power output associated with specific intensities expressed as $\%\dot{V}O_{2max}$ (Bouchard et al., 1999, Bouchard et al., 2011, Gaskill et al., 2001a, Pérusse et al., 2001). Bouchard et al. (1999) estimated that up to 47% of the inter-individual variability in $\dot{V}O_{2max}$ responses to training could be accounted for by genetics after adjustment for age, sex, and baseline $\dot{V}O_{2max}$. A subsequent examination of the same dataset likewise showed that 21 single-nucleotide polymorphisms account for 49% of the $\dot{V}O_{2max}$ response variability (Bouchard et al., 2011). In contrast, Gaskill et al. (2001a) arrived at race-specific heritability estimates of 22% (whites) and 51% (blacks) for GET, while the estimates of Pérusse et al. (2001) reached 57%, 23%, 44%, 33%, and 45% for the $\dot{V}O_2$ at 50 W, $\dot{V}O_2$ at $60\%\dot{V}O_{2max}$, $\dot{V}O_2$ at $80\%\dot{V}O_{2max}$, power output at $60\%\dot{V}O_{2max}$, and power output at $80\%\dot{V}O_{2max}$, respectively.

Even though the aforementioned twin and family studies suggest a strong link between genetics and the magnitude of adaptive responses, several findings cast doubt on this view. First, none of the single-nucleotide polymorphisms associated with $\dot{V}O_{2max}$ gains in the study of Bouchard et al. (2011) reached genome-wide significance (i.e. $P < 5 \times 10^{-8}$ to account for multiple testing in hypothesis-free genomic explorations (Chen et al., 2021)). Second, amongst the 15 single-nucleotide polymorphisms most strongly associated with $\dot{V}O_{2max}$ gains in the HERITAGE cohort of white individuals, only 5 were replicated across three other smaller cohorts (Bouchard et al., 2011). Third, the 11 single-nucleotide polymorphisms accounting for 23% of the $\dot{V}O_{2max}$ response variability in the investigation of Timmons et al. (2010) did not coincide with the 21 single-nucleotide polymorphisms accounting for 49% of

the $\dot{V}O_{2max}$ response variability in the report of Bouchard et al. (2011). Fourth, Rankinen et al. (2016) did not identify common genomic variants that distinguish elite endurance athletes from sedentary controls. Fifth, in a randomised cross-over study wherein pairs of monozygotic and dizygotic twins underwent three months of resistance and endurance training separated by a 3-month washout, the relative contribution of a shared environment to the adaptive variability of $\dot{V}O_{2max}$ was estimated as 43%, suggesting that the 0.45 intra-pair correlation amongst monozygotic twins may not be indicative of a strong genetic role as previously thought (Marsh et al., 2020).

Despite the emergence of new studies linking single-nucleotide polymorphisms to increased $\dot{V}O_{2max}$ (Bye et al., 2020, Williams et al., 2017), it is likely that the genetic influence upon a given adaptive response elicited by endurance training is manifested as the cumulative effect of multiple genes with tiny effect sizes (Bouchard, 2019, Joyner, 2019, Sarzynski et al., 2017). This may explain why there have been so many contradictions in heritability research.

2.4.2 – Sex and training adaptation

The literature on morphological and physiological sex differences leaves no doubt that men and women are different (Astrand, 1960, Astrand et al., 1973, Hunter, 2014, Janssen et al., 2000, Miller et al., 1993, Tate and Holtz, 1998). It is therefore not surprising that there is a performance gap between men and women across a range of endurance sports (Hill, 1925, Sandbakk et al., 2018, Thibault et al., 2010). Accordingly, one might question whether these structural and functional differences also lead to adaptive responses to endurance training that are sex-dependent in terms of magnitude.

Meyler et al. (2021) concluded that $\dot{V}O_{2max}$ increases resulting from endurance training are generally larger in men. However, they may have placed too much emphasis on a meta-analysis of 8 studies indicating that for a given training dose $\dot{V}O_{2max}$ gains differ between men and women by 191 $ml \cdot min^{-1}$ or 2 $ml \cdot kg^{-1} \cdot min^{-1}$ (Diaz-Canestro and Montero, 2019). Meyler et al. (2021) also cited the study of Howden et al. (2015), which was included in the meta-analysis of Diaz-Canestro and Montero (2019) and produced the largest sex difference. As a result of a 1-year endurance training programme, previously sedentary men (n = 7) progressively increased $\dot{V}O_{2max}$, left ventricle mass, and mean ventricle wall thickness, reaching a plateau from the ninth to the twelfth month (Howden et al., 2015). Despite a similar training programme, women (n = 5) had the same responses plateauing after only

three months, suggestive of a sex difference in both time course and magnitude of adaptations (Howden et al., 2015). While these studies provide strong evidence that men respond better to endurance training, it may be argued that the literature as a whole is not as clear-cut as to permit such a conclusion. After thoroughly reviewing the endurance training publications up to 1973, Pollock (1973) stated that "females adapt to training in the same manner as do males". More recently, a position stand of the American College of Sports Medicine concluded that sex has little influence on the adaptive variability observed following exercise training (Garber et al., 2011). Clearly, these and Meyler's (Meyler et al., 2021) narrative reviews are ultimately subject to bias. Thus, the results of large multi-centre studies may better reflect the state of knowledge.

In a sample of 287 men and 346 women of the HERITAGE family study, Skinner et al. (2001) reported that women increased $\dot{V}O_{2max}$ to a greater extent in percentage units of baseline. However, when changes were expressed in $ml \cdot min^{-1}$ and $ml \cdot kg^{-1} \cdot min^{-1}$, a larger increase for men and no between-sex difference were found, respectively (Skinner et al., 2001). In another investigation, Williams et al. (2019) pooled the data of 677 participants of 18 training studies and detected a sex difference for $\dot{V}O_{2max}$ responses to HIIT but not moderate-intensity continuous training. Specifically, men improved by 0.49 $L \cdot min^{-1}$ and women by only 0.15 $L \cdot min^{-1}$. However, when considering every training protocol together, the impact of sex was relatively small, given that the overall effect of all covariates examined (i.e. sex, age, individual study, study duration, training sessions per week, population group, and the average between pre- and post-training scores) accounted for 17% of the inter-individual variability in $\dot{V}O_{2max}$ changes, with individual studies alone accounting for 13.5%. Likewise, in a sample of 742 participants of the HERITAGE family study, sex has been estimated to account for only 3% of the variability in $\dot{V}O_{2max}$ gains with training (Sarzynski et al., 2017). Overall, the results of large multi-centre studies are, at best, contradictory, and the current evidence is tentative. Further studies are required to shed light on this topic before researchers are able to draw definitive conclusions.

2.4.3 – Age and training adaptation

For the purposes of this literature review, children and teenagers will not be considered. Young adults in their twenties will represent the first age group. The ageing process is generally characterised by a decrease in physiological capacity, which is particularly evident for $\dot{V}O_{2max}$, even amongst individuals that maintain lifelong exercise habits (Astrand, 1960,

Astrand et al., 1973, Grimsmo et al., 2010, Robinson et al., 1976, Valenzuela et al., 2020, Wilson and Tanaka, 2000). This means that once an individual reaches his/her age-related potential for a high $\dot{V}O_{2max}$ (Figure 2.9), trainability is likely to be diminished. Accordingly, it may be interpreted that trainability decreases with advancing age for any physiological parameter that worsens with age.

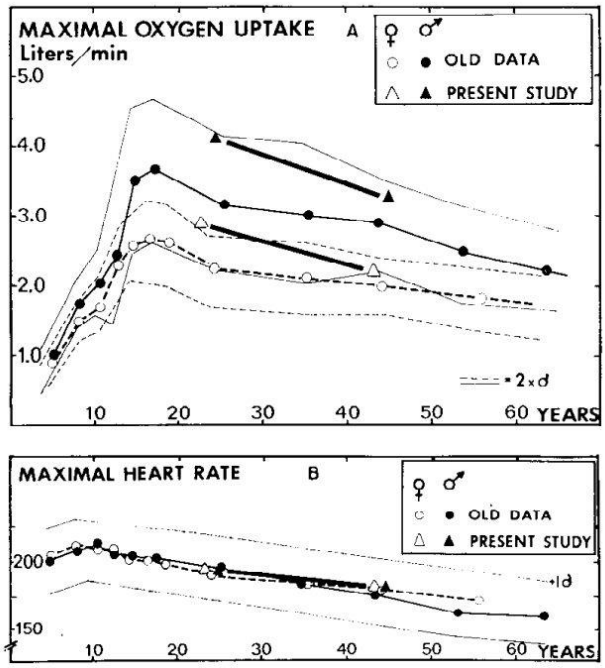

Figure 2.9 – Combined maximal oxygen uptake and heart rate data of 416 individuals measured during exercise on a treadmill or cycle ergometer. Taken from Astrand et al. (1973) p. 652.

From another perspective, physical activity levels also tend to decline with age (Bijnen et al., 1998, Sallis, 2000), which means that most people are far from reaching their age-related potential for a high $\dot{V}O_{2max}$. A question that arises is therefore whether ageing affects the trainability of typically sedentary individuals. From the age of twenty to sixty-three years, Saltin et al. (1969) noted that $\dot{V}O_{2max}$ changes with training are not affected by ageing when expressed in percentage units of baseline. There may be an effect, though, when changes are expressed in absolute terms (Saltin et al., 1969). Interestingly, the same observations were made by Skinner et al. (2001) from the analysis of the HERITAGE family study data. However, by combining their data (i.e. 633 men and women, aged 17 to 65 years) with the data of Kohrt et al. (1991) (i.e. 110 men and women, aged 60 to 71 years) to extend the age range analysed, Skinner et al. (2001) obtained a non-significant correlation coefficient of -

0.08 between age and $\dot{V}O_{2max}$ changes expressed in $ml \cdot kg^{-1} \cdot min^{-1}$. This finding led them to conclude that $\dot{V}O_{2max}$ responses to endurance training do not differ between old and young individuals. More recently, this view has been endorsed by the American College of Sports Medicine (Garber et al., 2011).

On the other hand, there is longitudinal evidence in favour of an ageing effect upon $\dot{V}O_{2max}$ trainability. This comes from a thirty-year follow-up (McGuire et al., 2001) of the classic Dallas Bed Rest and Training Study (Saltin et al., 1968). The 5 twenty-year-old individuals that took part in the original study involving three weeks of bed rest followed by eight weeks of endurance training (Saltin et al., 1968) underwent a second programme of six months in which the aim was to increase the training dose to the level achieved thirty years before (McGuire et al., 2001). Despite the fact that the HIIT sessions of the original programme were not reproduced, increases in $\dot{V}O_{2max}$ were similar when expressed in percentage units of baseline. But in contrast to the original study in which $\dot{V}O_{2max}$ gains were brought about by increases in both $\dot{Q}$ and a-$\overline{v}O_{2diff}$ (Saltin et al., 1968), the second training programme elicited a-$\overline{v}O_{2diff}$ improvements only (McGuire et al., 2001). These findings may suggest that the heart gradually loses its ability to adapt with ageing, analogous to the well-documented decline of HR_{max} throughout life (Astrand, 1960, Astrand et al., 1973, Wilson and Tanaka, 2000).

As the extent to which age accounts for $\dot{V}O_{2max}$ responses to training has varied from 1% to 16% between studies (Hautala et al., 2006, Hautala et al., 2003, Kohrt et al., 1991, Sarzynski et al., 2017, Skinner et al., 2001), potential effects of ageing upon $\dot{V}O_{2max}$ trainability have generally been considered minor (Meyler et al., 2021). If considered along with the trend of declining $\dot{V}O_{2max}$ across the lifespan (Astrand, 1960, Astrand et al., 1973, Grimsmo et al., 2010, Robinson et al., 1976, Valenzuela et al., 2020, Wilson and Tanaka, 2000), it may be justifiable to assume that old individuals do not respond to endurance training as well as young adults.

2.4.4 – Initial fitness and training adaptation

From the observation that elite endurance athletes experience few changes in $\dot{V}O_{2max}$ throughout their careers once a high level is reached (Ekblom, 1969, Jones, 1998, Lundby and Robach, 2015), coupled with the decline in $\dot{V}O_{2max}$ that even the best athletes of each age group manifest (Valenzuela et al., 2020), it becomes obvious that trainability diminishes

once the genetic potential of an individual is approached. Indeed, it has been suggested that for these highly trained athletes, with a solid base of low-intensity training, only HIIT may be able to promote further, albeit small, training adaptations (Laursen and Jenkins, 2002, Midgley et al., 2006, Seiler and Tønnessen, 2009). That said, it is of interest to answer the question of whether there is a relationship between trainability and baseline fitness levels for individuals that have yet to approach their best.

By making use of different datasets, Saltin (1969) concluded that percentage improvements of $\dot{V}O_{2max}$ are highly dependent on its baseline level (Figure 2.10). Pollock (1973) reviewed a vast literature and arrived at a similar conclusion. Interestingly, Wenger and Bell (1986) went on to suggest that also absolute changes in $\dot{V}O_{2max}$ are dependent on initial fitness levels irrespective of training intensity, duration, and frequency. More recently, a position stand of the American College of Sports Medicine stated that there is a minimal intensity threshold that must be surpassed during training to promote adaptations, although this threshold may be dependent on initial fitness (Garber et al., 2011). This conclusion was primarily driven by the findings of Swain and Franklin (2002). They reviewed 18 training studies and identified that individuals with baseline $\dot{V}O_{2max}$ of 40 $ml \cdot kg^{-1} \cdot min^{-1}$ or higher required an intensity of at least 45% of $\dot{V}O_2$ reserve (45%$\dot{V}O_{2reserve}$) to demonstrate $\dot{V}O_{2max}$ improvements, whereas those with lower fitness could improve with any intensity above 30%$\dot{V}O_{2reserve}$ (Swain and Franklin, 2002). The compilation of results of several studies thus looks very clear: $\dot{V}O_{2max}$ trainability diminishes as baseline fitness increases.

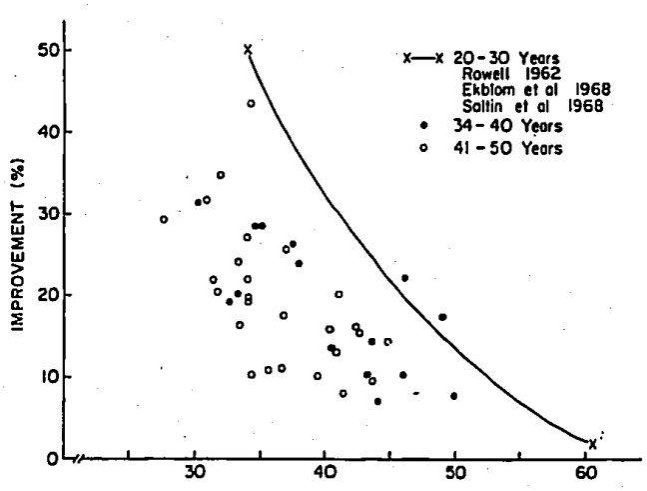

Figure 2.10 – Relationship between the percentage improvement of maximal oxygen uptake with training (y-axis) and its baseline at the start of the programme (x-axis). Taken from Saltin (1969) p. 55.

However, the data of the HERITAGE family study suggests that only 2% of the inter-individual variability in $\dot{V}O_{2max}$ changes ($ml \cdot min^{-1}$) are associated with the $\dot{V}O_{2max}$ measured before the start of the training programme (Sarzynski et al., 2017). Moreover, Skinner et al. (2001) found a non-significant correlation of 0.08 between $\dot{V}O_{2max}$ changes and baseline $\dot{V}O_{2max}$, both in $ml \cdot kg^{-1} \cdot min^{-1}$, although it must be acknowledged that a significant correlation of -0.38 was detected when changes were expressed as percentage units of baseline. Getting into the details of each study thus seems necessary.

If on one hand, the age range of the HERITAGE family study participants (i.e. 17 to 65 years) may have confounded the analysis of other potential predictors of $\dot{V}O_{2max}$ changes such as initial fitness (see Section 2.4.3 – Age and training adaptation), on the other, previous research as reviewed by Saltin (1969), Pollock (1973), Wenger and Bell (1986), and Garber et al. (2011) may have suffered from statistical issues. Specifically, correlational analysis involving changes in a variable and its baseline value may be subject to "regression to the mean" and "mathematical coupling" artefacts (Atkinson and Batterham, 2015, Tu and Gilthorpe, 2007). It is therefore possible to question whether initial fitness level indeed affects adaptive responses to training. While this relationship makes sense in light of the overload principle (Hellebrandt and Houtz, 1956, Müller, 1962), further research with large samples and statistically sound methods is required to shed light on this topic.

2.4.5 – Exercise intensity as a source of variability

Exercise intensity has traditionally been expressed as $\%\dot{V}O_{2max}$ (e.g. Åstrand and Ryhming (1954)) based on the premise that the cardiorespiratory and muscle strain experienced by an individual during exercise reflects a) the $\dot{V}O_2$ elicited, as a physiological manifestation of the rate of work output, and b) how far that $\dot{V}O_2$ is from the individual's $\dot{V}O_{2max}$ (Astrand, 1967, Ekblom et al., 1968, Saha et al., 1979). Due to the quasi-linear relationship between $\dot{V}O_2$ and work rate (Hansen et al., 1988, Iannetta et al., 2019a), the power output or running speed associated with a given $\%\dot{V}O_{2max}$ may be obtained for each individual and used for intensity prescription (Iannetta et al., 2019a, Keir et al., 2018). Because there is also a quasi-linear relationship between HR and $\dot{V}O_2$ (Karvonen and Vuorimaa, 1988, Marini et al., 2021, Wyndham et al., 1959), HR can be alternatively used to target a given $\%\dot{V}O_{2max}$ under conditions of steady-state exercise with little thermoregulatory stress and fatigue (Achten and Jeukendrup, 2003, Karvonen and Vuorimaa, 1988, Lambert et al., 1998).

Despite the popularity of these methods (Garber et al., 2011, Howley, 2001, Jamnick et al., 2020, Mann et al., 2013), several studies have contributed to a growing consensus that %$\dot{V}O_{2max}$, or its derivative %HR_{max}, should be avoided for exercise intensity prescription (Coyle et al., 1988, Egger et al., 2016, Iannetta et al., 2020, Jamnick et al., 2020, Katch et al., 1978, Lansley et al., 2011, Mann et al., 2013, Scharhag-Rosenberger et al., 2010). For instance, Iannetta et al. (2020) analysed the data of 100 individuals to demonstrate that both GET and the maximal lactate steady state, representing the boundaries of three exercise intensity domains (i.e. moderate, heavy, and very heavy) (Rossiter, 2011), occur at a wide %$\dot{V}O_{2max}$ range (GET: 45–74%; maximal lactate steady state: 69–96%). Thus, prescribing exercise to a group of individuals at intensities within 55–65%$\dot{V}O_{2max}$ and 75–85%$\dot{V}O_{2max}$ is very likely to result in inter-individual differences in the domain allocation of training (Iannetta et al., 2020), which is indicative of a flawed intensity normalisation (Jamnick et al., 2020, Mann et al., 2013, Meyler et al., 2021), given that many physiological and metabolic responses to exercise are domain-specific (Black et al., 2017, Jamnick et al., 2020, Rossiter, 2011). Yet, the publications more frequently associated with inter-individual variability in adaptive responses to training reported data from the HERITAGE family study (Bouchard et al., 1999, Bouchard and Rankinen, 2001), in which selected %$\dot{V}O_{2max}$ were prescribed via HR (Bouchard et al., 1995). Likewise, %$\dot{V}O_{2max}$ and %HR_{max} have been used in more recent studies wherein a large adaptive variability between individuals was highlighted (Bonafiglia et al., 2016, Del Giudice et al., 2020, Marsh et al., 2020, Maturana et al., 2021, Ross et al., 2015, Vollaard et al., 2009, Williams et al., 2019). It is therefore possible to question the extent to which inter-individual variability in training adaptations resulted from variability in the adaptive stimulus that each participant received (Iannetta et al., 2020, Mann et al., 2014, Meyler et al., 2021, Vollaard et al., 2009). In other words, the training dose may not have been standardised as assumed by authors (Bonafiglia et al., 2016, Bouchard et al., 1995, Del Giudice et al., 2020, Marsh et al., 2020, Maturana et al., 2021, Ross et al., 2015, Vollaard et al., 2009, Williams et al., 2019).

It is important to note, however, that the evidence for a direct link between inter-individual variability in training adaptations and how exercise intensity is normalised is contradictory. Most often, the comparison between groups that differ in how exercise intensity is normalised does not seem to reveal differences in the magnitude of adaptive variability (Johnson et al., 2017, McLellan and Skinner, 1981, Preobrazenski et al., 2019, Swart et al., 2009). McLellan and Skinner (1981) recruited 14 sedentary individuals for a training

intervention involving thrice-weekly continuous exercise, lasting 30 to 45 min, and progressing in intensity from approximately 55% to 65%$\dot{V}O_{2max}$. Eight participants were allocated to the %$\dot{V}O_{2max}$ group, and six were allocated to the %GET group. How exercise intensity was normalised across individuals differed between groups, but they trained at similar power outputs on average. In contrast to the authors' hypothesis, the magnitude of inter-individual variability in $\dot{V}O_{2max}$ changes was similar between groups (McLellan and Skinner, 1981). Comparable results were presented by Swart et al. (2009), Johnson et al. (2017), and Preobrazenski et al. (2019), who respectively split individuals into two groups training at 80%$\dot{W}_{max}$ or the HR associated with 80%$\dot{W}_{max}$, at the rating of perceived exertion (RPE) or HR associated with selected %$\dot{V}O_{2reserve}$, and at 65%$\dot{W}_{max}$ or the first negative stage of the talk test (see Reed and Pipe (2014) for talk test details). Overall, these studies do not corroborate the assumption that adaptive variability can be minimised depending on the method chosen for training intensity normalisation.

Interestingly, Weatherwax et al. (2019) and Wolpern et al. (2015) concluded that how exercise intensity is normalised affects the incidence of non-response to training for $\dot{V}O_{2max}$. By splitting participants into two groups, they compared the %$HR_{reserve}$ method with an individualised approach using the HR associated with each ventilatory threshold for consistent allocation of training into intensity domains. While all individuals of the individualised approach groups increased $\dot{V}O_{2max}$ by more than 4.7% and 5.9% (i.e. the responder threshold set for each study), approximately half of the %$HR_{reserve}$ groups did not (Weatherwax et al., 2019, Wolpern et al., 2015). Accordingly, these studies have been cited as evidence for the intensity prescription method being the driver of adaptive variability (Iannetta et al., 2020, Jamnick et al., 2020, Meyler et al., 2021). However, a detailed inspection reveals that outcomes were affected by the higher average intensity of the individualised approach, as indicated by group differences in training heart rate of more than 10 beats.min^{-1}, which also led to larger average $\dot{V}O_{2max}$ gains. This suggests that Weatherwax et al. (2019) and Wolpern et al. (2015) failed to isolate the effect of the intensity prescription method from the effect of training intensity. Besides, it may be argued that both groups actually responded similarly to the training intervention in terms of magnitude of inter-individual variability (Weatherwax et al., 2019, Wolpern et al., 2015), with the incidence of non-response reflecting the mean adaptive changes rather than the non-response itself, as empirically demonstrated by Atkinson et al. (2019). Increase the mean $\dot{V}O_{2max}$ gain enough,

and the left tail of a normal distribution, that is, the non-responders, will always surpass a given cut-off value, becoming responders (Atkinson et al., 2019).

In contrast with the aforementioned findings, the study of Preobrazenski et al. (2019) demonstrated that the mean [La^-] of the first session of the training programme was positively correlated with the $\dot{V}O_{2max}$ changes within a group that trained at 65%$\dot{W}_{max}$. This implies that, for a "standardised" training dose, those individuals that manifested the highest levels of metabolic stress during exercise improved their fitness more. Likewise, Gaskill et al. (2001c) reported that training intensity in the HERITAGE family study, originally normalised as %$\dot{V}O_{2max}$ (Bouchard et al., 1995), accounted for 26% of the gains in the $\dot{V}O_2$ associated with GET when expressed as %GET. In other words, the higher the intensity relative to GET was, the higher the GET gain was (Gaskill et al., 2001c). On the other hand, intensity expressed as %GET did not account for the magnitude of $\dot{V}O_{2max}$ changes, which reduces somewhat the strength of this evidence.

Altogether, the evidence points to a possible role of exercise intensity, or more precisely, the method used for its normalisation, as a source of inter-individual variability in training adaptations. However, the evidence is contradictory even among the findings of the largest study on the topic (Gaskill et al., 2001c), suggesting that more studies are required to shed light on this topic.

2.4.6 – Non-response to training

Since the seminal report of Bouchard (1983), it became apparent that a few individuals manifest very little adaptive responses to endurance training, from submaximal and maximal cardiorespiratory parameters to direct measures of performance. Because the inter-individual variability observed by Bouchard (1983) could not be accounted for by age, sex, prior training experience, and baseline fitness, he reasoned that adaptive responses to training must be greatly affected by genetics. This led to a series of investigations in which the magnitude of inter-individual variability in various adaptive responses was highlighted (Boulay et al., 1986, Hamel et al., 1986, Lortie et al., 1984, Prud'homme et al., 1984, Simoneau et al., 1986). However, it was only after Bouchard et al. (1999) published a report on the large HERITAGE family study that the notion of non-response to training became widely recognised. They demonstrated that, out of 481 previously sedentary individuals,

more than 30 failed to improve $\dot{V}O_{2max}$ by more than 100 ml·min^{-1} following 20-weeks of endurance training, with some individuals even manifesting negative changes.

Ever since, the term non-responder has often been used to designate those individuals that fail to improve a particular parameter with training (Astorino and Schubert, 2014, Bonafiglia et al., 2019b, Bouchard et al., 1999, Coakley and Passfield, 2018b, Hecksteden et al., 2018b, Maturana et al., 2021, Scharhag-Rosenberger et al., 2012, Sisson et al., 2009). However, several researchers have criticised this term and challenged the notion of non-response (Booth and Laye, 2010, Joyner and Lundby, 2018, Mann et al., 2014, Pickering and Kiely, 2019). The reasons are severalfold. First, a non-responder for one parameter (e.g. $\dot{V}O_{2max}$) may respond pretty well for another parameter (e.g. time-trial performance) (Astorino and Schubert, 2014, Barber et al., 2021, Bonafiglia et al., 2016, Coakley and Passfield, 2018b, Lortie et al., 1984, Vollaard et al., 2009). Second, non-response to training may be modality- (i.e. endurance versus resistance training) (Hautala et al., 2006, Marsh et al., 2020), volume- (Montero and Lundby, 2017, Ross et al., 2015, Sisson et al., 2009), and intensity-dependent (Bonafiglia et al., 2016, Coakley and Passfield, 2018b, Maturana et al., 2021, Ross et al., 2015, Williams et al., 2019). Third, non-response to training may be considered large and universal or small and non-existent depending on the statistical methods chosen for its quantification (Atkinson and Batterham, 2015, Bonafiglia et al., 2019b, Hecksteden et al., 2018b, Hopkins, 2018, Ross et al., 2019, Shephard et al., 2004, Swinton et al., 2018, Voisin et al., 2019). Fourth, non-response may result from some individuals receiving sub-optimal training stimulus due to methodological problems with how exercise intensity is normalised (Mann et al., 2014, Meyler et al., 2021) (see Section 2.4.5 – Exercise intensity as a source of variability). Fifth, and lastly, adaptive responses may be subject to a great level of intra-individual variability when the same training programme is repeated on distinct occasions (Cureton and Phillips, 1964, Del Giudice et al., 2020, Örlander et al., 1977, Pedersen and Jørgensen, 1978). While Booth and Laye (2010) have proposed the term low-sensitivity responder to address the first and second reasons, the third, fourth, and fifth reasons suggest this is not just a matter of semantics. The evidence therefore indicates that a dichotomous classification of individual responses to training is difficult to achieve with certainty, if not an unrealistic target, applying only under the narrow set of circumstances within the investigation.

2.5 – Methods of intensity prescription

In 1978, Katch et al. (1978) demonstrated that if training was prescribed at 80%HR_{max}, there would be large inter-individual variability in terms of %$\dot{V}O_{2max}$ (62.5 ± 7.9) and %GET (106.6 ± 15.9), with 17 individuals exercising above and 14 individuals exercising below GET. Accordingly, Katch et al. (1978) stated that "indiscriminate use of the relative percent concept, as typically used to equate physical training stimuli may result in erroneous experimental conclusions". They also proposed that GET should be used as a benchmark for the normalisation of exercise intensity (Katch et al., 1978).

Surprisingly, 33 years later, the American College of Sports Medicine published a position stand with exercise intensity guidelines based on %$\dot{V}O_{2max}$ and %HR_{max}, among other intensity benchmarks (Garber et al., 2011). It is thus understandable that researchers will continue to adopt ineffective methods for exercise intensity normalisation (Bonafiglia et al., 2016, Del Giudice et al., 2020, Marsh et al., 2020, Maturana et al., 2021, Ross et al., 2015, Williams et al., 2019). Fortunately, the normalisation of exercise intensity has become a hot topic recently (Beck et al., 2018, Iannetta et al., 2020, Jamnick et al., 2020, Keir et al., 2018, Mann et al., 2013, Mann et al., 2014, Marini et al., 2021, Meyler et al., 2021, Weatherwax et al., 2019), which is the first step to promote alternative and potentially better methods. Nevertheless, several researchers have addressed this topic decades earlier, and their contribution should not be overlooked if novel prescription solutions are to be developed (McLellan, 2011).

2.5.1 – Performance-based methods

In a review of the history of HIIT, Billat (2001) noted that athletes and coaches have often used the average racing speed over certain standard distances (e.g. 5000 m) to "calibrate" the intensity of training (e.g. 4 × 400m at 96% of 5000-m speed), whereas researchers have generally preferred to express training intensity as %$\dot{V}O_{2max}$ (including herself, Daniels and Scardina (1984), and Saltin et al. (1976)). While the predominance of %$\dot{V}O_{2max}$ among scientists is undeniable (Garber et al., 2011, Howley, 2001, Jamnick et al., 2020, Mann et al., 2013), there have been a few exceptions.

Nordesjö (1974) departed from tradition and conducted a training study wherein the intensity of exercise was normalised as a percentage of the maximal work rate estimated for a given session duration. Participants cycled to exhaustion at constant power outputs to establish

individual relationships between the logarithm of work rate and the logarithm of time. Accordingly, the training intervention was prescribed as 50%, 75%, and 100% of the maximal sustainable work rate predicted for 15, 60, and 120 min of exercise (Nordesjö, 1974). More recently, a similar concept has been put forward by Hofmann and Tschakert (2017), wherein percentages of the maximal duration associated with a given work rate are prescribed, with intensity domains serving as a backdrop for work rate selection. Although these performance-based approaches are likely more recognisable to athletes as suggested by Billat (2001), there is little evidence to support their use over more traditional methods such as $\%\dot{V}O_{2max}$. One reason might be the difficulty in persuading well-trained research participants, for whom testing is less likely to affect performance, to undertake maximal efforts for extended durations either to establish reliable work rate-time relationships or to assess the accuracy of derived equations.

While the comparison between methods is ultimately necessary to establish the best options for intensity normalisation, the data reported by Nordesjö (1974) may provide some clues as to the "quality" of his training prescriptions. For predicted TTEs of 6 and 90 min, participants cycled for 6.0 ± 1.5 and 92.5 ± 28.3 min, respectively, yielding inter-individual CVs of 25.0% and 30.6%. Similarly, in the study of Faude et al. (2017) cycling to exhaustion was performed at the maximal lactate steady state and participants lasted 50.8 ± 14.0 and 48.2 ± 16.7 min in the first and second attempts, respectively, yielding inter-individual CVs of 27.6% and 34.6%. Given that the maximal lactate steady state has been considered a physiological benchmark that differentiates steady from non-steady metabolic states during continuous exercise (Billat et al., 2003, Faude et al., 2009), although not without controversy (Jones et al., 2019), the performance variability reported by Nordesjö (1974) may be considered acceptable despite its large magnitude.

A popular strategy for exercise intensity prescription based on performance is through the parameters of the two-parameter CP model (i.e. CP and W'; see Figure 2.11) (Jones and Vanhatalo, 2017, Pettitt, 2016, Vanhatalo et al., 2011). The principle is the same as for the aforementioned methods (i.e. based upon the highest sustainable work rate for a given duration). The CP model was first described by Monod and Scherrer (1965), who investigated the hyperbolic relationship between power output and time for which it can be sustained for small muscle groups. They noted that prolonged muscular activity that does not involve fatigue could only be achieved when performed below what they called CP

(Monod and Scherrer, 1965). The same model was later applied to cycling exercise and CP was shown to be highly correlated with GET (Moritani et al., 1981). Today, it is understood that CP separates the heavy from the very heavy intensity domains (Jones and Vanhatalo, 2017, Poole et al., 1988, Rossiter, 2011), with some authors considering it the gold standard measure, rather than the maximal lactate steady state, that differentiates steady from non-steady metabolic states during continuous exercise (Jones et al., 2019). While there have been various attempts to attribute physiological significance to both CP and W' (Poole et al., 2016, Vanhatalo et al., 2016, Vanhatalo et al., 2010), this model of intensity prescription is ultimately based upon a mathematical relationship that characterises performance.

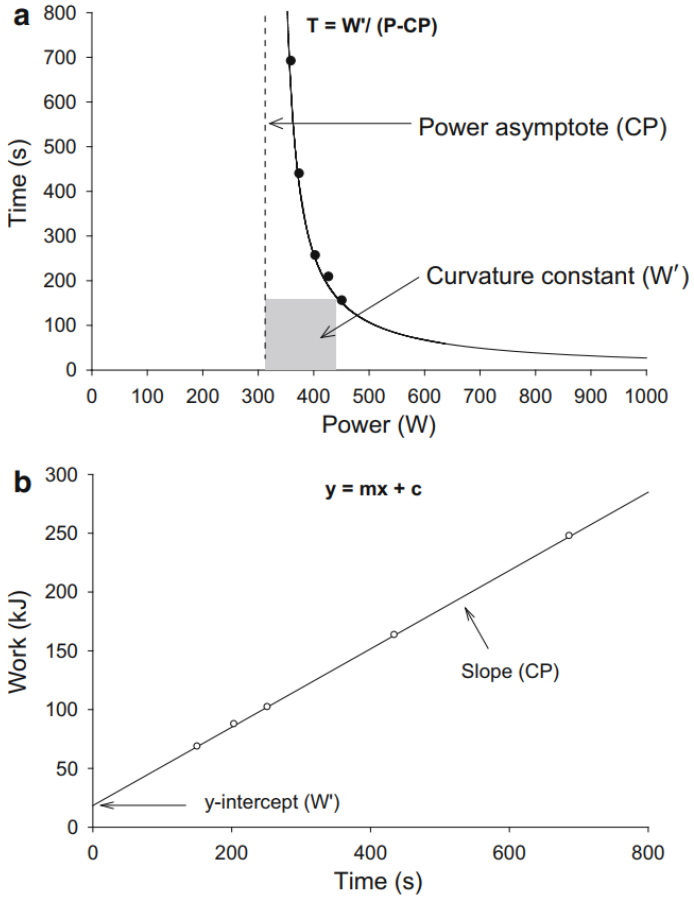

Figure 2.11 – The top panel describes the hyperbolic relationship between time to exhaustion (y-axis) and the power output at which exercise is performed (x-axis). The power asymptote represents the critical power (CP) and the curvature constant represents the work capacity above critical power (W'). The bottom panel describes the linear relationship between work accomplished (y-axis) and time to exhaustion (x-axis) in which CP is represented by the slope of the line and W' by its intercept. Taken from Jones and Vanhatalo (2017) p. S66.

With personal estimates of CP and W', it is possible to predict the maximal work rate sustainable for a given duration, or the TTE at a given work rate (Jones and Vanhatalo, 2017, Pettitt, 2016, Vanhatalo et al., 2011). However, Hill (1993) has argued that the validity of the CP model is restricted to exercise intensities that lead to exhaustion in between 1 and 40 min. In fact, this range may be even narrower, given that Muniz-Pumares et al. (2019) have recommended that preliminary trials last 2 to 15 min if the model is to be accurate. As a rule of thumb, the applicability of the two-parameter CP model may be restricted to exercise durations of 1 to 20 min, which is the range typically considered for the evaluation of different modelling approaches (Gaesser et al., 1995, Maturana et al., 2018).

There have been several studies in which the predictive ability of the two-parameter CP model was assessed. In the study of Housh et al. (1989), TTE tests were conducted at 97%, 120%, 140%, and 160%CP. Although the CP model could not be used to predict TTE at 97%CP, exercise was theoretically expected to last for much longer than the actual 33.3 ± 15.4 min. On the other hand, the model proved accurate for 120%, 140%, and 160%CP, in which TTEs were 8.2 ± 3.9, 3.6 ± 1.4, and 2.4 ± 1.0 min, respectively, with no significant differences from predicted times. Standard errors of estimate of 1.2, 0.6, and 0.4 min were obtained for respectively the 120%, 140%, and 160%CP trials, representing approximately 15% of the mean trial duration. In the study of Pepper et al. (1992), a similar experimental design was adopted, but critical speed (CS) and distance capacity above CS (D') were modelled (i.e. running based equivalents of CP and W', respectively). TTE tests were conducted at 100%, 115%, and 130%CS. At 100%CS, again, participants ran for much shorter (16.4 ± 6.1 min) than would be expected from a theoretical point of view. At 115%CS, predicted (7.2 ± 3.0 min) and actual times (7.2 ± 2.8 min) to exhaustion were similar, whereas at 130%CS there was a significant difference (predicted: 3.2 ± 1.3 min; actual: 3.4 ± 1.4 min). Standard errors of estimate of 0.8 and 0.3 min were obtained for respectively the 115% and 130%CS trials, representing approximately 10% of the mean trial duration. More recently, Pallarés et al. (2020) reported that predicted (3.3 ± 0.5 min) and actual TTEs (3.4 ± 0.8 min) were similar at the power output associated with $\dot{V}O_{2max}$. In contrast, the CP model overestimated (52 ± 12 s) the actual TTEs (29 ± 6 s) at the mean power output of a Wingate test (see Bar-Or (1987) for details), and underestimated (7.2 ± 2.5 min) the actual TTEs (11.5 ± 5.1 min) at RCP. Standard errors of estimate were not presented though. While other researchers have also attempted to address the predictive value of the CP model, results tend to converge (Chidnok et al., 2013a, Ferguson et al., 2010,

Kennedy and Bell, 2000). Altogether, the two-parameter CP model appears to be reliable, but predictions may be way off the mark depending on the methods utilised for model fitting and the expected durations over which exercise is to be performed (Gaesser et al., 1995, Hill, 1993, Maturana et al., 2018, Muniz-Pumares et al., 2019).

It is evident that, besides the two-parameter CP model, various mathematical formulations, including a three-parameter CP model (Morton, 1996), can be used to derive individual work rate-time relationships as reviewed by Billat et al. (1999a). These models can be subsequently applied for the prescription of exercise intensity. However, there have been few studies that published data on the precision of predictions derived from models other than the CP. One exception is the study of Nicolò et al. (2019), in which they used TTE tests at approximately 70%, 76%, and 87%$\dot{W}_{max}$ to derive individual work rate-time relationships using a power-law function (see García-Manso et al. (2012) for details). Nicolò et al. (2019) subsequently required participants to cycle to exhaustion at work rates predicted to be endured for 20 min, in which they actually attained 22.0 ± 5.9 min, yielding an inter-individual CV of 26.8%. While it is difficult to compare results between studies that used rather different methods, this magnitude of inter-individual variability is similar to those estimates obtained by Nordesjö (1974) and Faude et al. (2017). Future studies are required to compare methods for exercise intensity prescription on the basis of distinct performance modelling formulations.

All the methods of intensity prescription mentioned above rely on model-fitting procedures. However, it has also been a common practice to express exercise intensity as a percentage of a single performance parameter, such as $\dot{W}_{max}$ (Granata et al., 2018, Iannetta et al., 2020, Jamnick et al., 2020) or the average power output of a time-trial (see below). Similar to %$\dot{V}O_{2max}$, %$\dot{W}_{max}$ is likely to cause inter-individual variability in the (intensity) domain allocation of training (Iannetta et al., 2020). Nevertheless, it must be noted that in the study of Bentley et al. (2007a), in which exercise was performed at 75% and 85%$\dot{W}_{max}$ for 20 and 90 min, respectively, there were no metabolic response differences (e.g. [La^{-}]) between two groups of trained cyclists of similar $\dot{W}_{max}$, but with lactate threshold occurring at different %$\dot{W}_{max}$. This study may therefore suggest that %$\dot{W}_{max}$ is an effective method of exercise intensity normalisation because the trials of each group were performed at different intensities relative to the lactate threshold (i.e. a rough estimate of the transition between the moderate and heavy intensity domains (Faude et al., 2009, Jamnick et al., 2020)). Further

studies are therefore required to confirm the utility of $\%\dot{W}_{max}$ as a method of exercise intensity prescription.

With the widespread use of power meters in the last two decades (Maier et al., 2017, Passfield et al., 2017, Sanders et al., 2020), and the more recent popularity of direct-drive "smart" trainers (McIlroy et al., 2021), some lay publications on cycling performance have received great attention (Allen and Coggan, 2010, Carmichael and Rutberg, 2009). In these books, Carmichael and Rutberg (2009) and Allen and Coggan (2010) proposed that the average power output produced in 8- and 20-min time-trials, respectively, could be used for performance monitoring and demarcation of training zones (i.e. a less stringent form of intensity prescription). Due to the large acceptance of these methods among coaches and athletes, both the 8- (Klika et al., 2007, Sanders et al., 2020) and 20-min time-trials (Barranco-Gil et al., 2020, Borszcz et al., 2018, Inglis et al., 2019, Morgan et al., 2019, Nimmerichter et al., 2011) made their way into the scientific literature. Nevertheless, most of the research concerns the ability to predict more established thresholds of intensity domain transition (Barranco-Gil et al., 2020, Borszcz et al., 2018, Inglis et al., 2019, Morgan et al., 2019, Sanders et al., 2020), while less attention has been directed to the performance in these tests as a benchmark for intensity prescription (Klika et al., 2007) and interpretation (Nimmerichter et al., 2011). It is therefore yet to be determined if time-trial performances can be used to normalise exercise intensity.

Finally, another possibility to normalise exercise intensity based upon performance is to make use of the peak (or average) power output (or speed) reached during a short all-out effort in combination with a parameter that is typically associated with aerobic exercise capacity. For instance, Barnett et al. (1996) assessed the inter-individual variability in TTE after participants cycled at $120\%\dot{V}O_{2max}$, 6 $W \cdot kg^{-1}$, $100\%\dot{V}O_{2max}$ plus 10% of the difference between peak power output and $100\%\dot{V}O_{2max}$ ($\dot{V}O_{2max}+10\%_{PPO\text{-}\dot{V}O2max}$), and $100\%\dot{V}O_{2max}$ plus 20% of the difference between the average power output in a 30-s all-out effort and $100\%\dot{V}O_{2max}$ ($\dot{V}O_{2max}+20\%_{APO\text{-}\dot{V}O2max}$). TTEs were not significantly different between conditions, with a grand mean of 163 s. However, the inter-individual CVs of 32.9%, 58.2%, 22.9%, and 15.0% for $120\%\dot{V}O_{2max}$, 6 $W \cdot kg^{-1}$, $\dot{V}O_{2max}+10\%_{PPO\text{-}\dot{V}O2max}$, and $\dot{V}O_{2max}+20\%_{APO\text{-}\dot{V}O2max}$, respectively, led Barnett et al. (1996) to conclude that expressing exercise intensity as $\dot{V}O_{2max}+20\%_{APO\text{-}\dot{V}O2max}$ would be the best option for maximal efforts of 2 to 3 min. In another study, Blondel et al. (2001) required individuals to run at 90%, 100%, 120%, and

140%$\dot{V}O_{2max}$ to elucidate whether alternative expressions of exercise intensity would better account for the inter-individual variability in TTE. Intensity was expressed as percentages of the difference between peak speed and CS (%$_{PS-CS}$), percentages of the difference between peak speed and the speed associated with $\dot{V}O_{2max}$ (%$_{PS-\dot{V}O2max}$), and percentages of the difference between the speed associated with $\dot{V}O_{2max}$ and CS (%$_{\dot{V}O2max-CS}$). For runs at 90% and 100%$\dot{V}O_{2max}$, the inter-individual variability in TTE was best accounted by expressing intensity as %$_{PS-CS}$. However, for runs at 120% and 140%$\dot{V}O_{2max}$, the variability in TTE was best accounted by %$_{PS-\dot{V}O2max}$. Accordingly, Blondel et al. (2001) concluded that the prescription of exercise intensity should be made on the basis of %$_{PS-CS}$ or %$_{PS-\dot{V}O2max}$ depending on the targeted intensity (i.e. below or above 100%$\dot{V}O_{2max}$). While more studies are required to confirm the utility of these methods of intensity normalisation, the combination of peak power output (or speed) and power output (or speed) associated with $\dot{V}O_{2max}$ ($\dot{V}O_{2max}$+10%$_{PPO-\dot{V}O2max}$ and %$_{PS-\dot{V}O2max}$ in the examples above) seems to be the most promising, giving that these variables have been used to model the performance of short duration efforts with generally good precision (i.e. $R^2 \geq 0.9$) (Bundle et al., 2003, Sanders and Heijboer, 2019, Sanders et al., 2017).

2.5.2 – Physiology-based methods

The most emblematic method of exercise intensity expression is %$\dot{V}O_{2max}$. Its origin is somewhat obscure, but it may be attributed to the work of Herbst (1928) who plotted 4.8-km running performances against the fraction of the $\dot{V}O_2$ estimated for the exercise task (although not exactly %$\dot{V}O_{2max}$). Later, Robinson (1938) plotted the kinetics of $\dot{V}O_2$ as %$\dot{V}O_{2max}$ to describe the transition from rest to maximal exercise. However, this standard for the expression of exercise intensity was likely consolidated only after the work of Åstrand and Ryhming (1954), in which the relationship between HR and %$\dot{V}O_{2max}$ served as the basis for the creation of a nomogram for $\dot{V}O_{2max}$ prediction.

In the last few decades, %$\dot{V}O_{2max}$ has also been used for exercise prescription (Garber et al., 2011, Howley, 2001, Jamnick et al., 2020, Mann et al., 2013). However, it has been a while since the publication of the first critiques of this approach. In 1978, Katch et al. (1978) manifested concerns regarding the assumed linearity between %HR_{max} and %$\dot{V}O_{2max}$ due to the work rate and time dependency of this relationship, as data are typically recorded continuously during incremental exercise tests. Moreover, Katch et al. (1978) cautioned against the indiscriminate use of %HR_{max}, given that neither %$\dot{V}O_{2max}$ nor %GET would be

similar between individuals if exercise was prescribed at 80%HR_{max}. In 1990, Weltman et al. (1990) extended the findings of Katch et al. (1978) by showing that at selected %HR_{max}, %$HR_{reserve}$, or %$\dot{V}O_{2max}$, there was often a similar proportion of runners whom [La^{-}] was below and above certain values (i.e. 2.0, 2.5, and 4.0 $mmol \cdot L^{-1}$), suggesting a large inter-individual variability in metabolic responses. Later, studies with similar experimental designs, but different analytical procedures, corroborated the initial findings (Iannetta et al., 2020, Marini et al., 2021, Meyer et al., 1999). Crucially, Iannetta et al. (2020) demonstrated that, in a large sample of 54 men and 46 women, GET and the maximal lactate steady state, representing the boundaries of intensity domains (i.e. moderate, heavy, and very heavy) (Rossiter, 2011), occurred at wide %$\dot{V}O_{2max}$ and %HR_{max} ranges. According with the principle that exercise prescriptions should take into consideration the intensity domains in order to elicit common physiological stress profiles (Jamnick et al., 2020, Mann et al., 2013, Meyler et al., 2021, Rossiter, 2011), the work of Iannetta et al. (2020) may represent the strongest evidence against the use of %$\dot{V}O_{2max}$ and %HR_{max}.

From a quantitative perspective, it may be argued that the optimal method of intensity prescription is the one which elicits low inter-individual variability in performance, physiological, and perceptual responses to exercise, irrespective of the domain allocation of training. This is not to neglect the existence of intensity domains or their importance for exercise prescription. Rather, this approach takes into account the fact that domain boundaries may be actually manifested as a continuum (Pethick et al., 2020), in addition to being subject to day-to-day biological variability and measurement error, regardless of the index chosen to represent each of the boundaries (e.g. maximal lactate steady state versus CP) (Gaskill et al., 2001b, Hauser et al., 2013, Lourenço et al., 2011, Pallarés et al., 2016, Smith and Hill, 1993). Accordingly, several investigations have been conducted to inform the topic of intensity normalisation by reporting inter-individual variability in acute exercise responses (Baldwin et al., 2000, Coyle et al., 1988, Egger et al., 2016, Gass et al., 1991, Lansley et al., 2011, McLellan and Gass, 1989, McLellan and Jacobs, 1991, McLellan and Skinner, 1985, Scharhag-Rosenberger et al., 2010).

McLellan and Skinner (1985) investigated the best intensity expression to estimate the logarithm of TTE when exercise was performed continuously at 75%, 85%, and 95%$\dot{V}O_{2max}$. The intensity expressions analysed included %$\dot{V}O_{2max}$ itself and two different expressions of %Δ in which either GET and $\dot{V}O_{2max}$ or GET, RCP, and $\dot{V}O_{2max}$ are considered together

(see Table 2.2). With standard errors of estimate decreasing, and coefficients of determination increasing (from 0.85 to 0.93), the more variables were included in the expression of intensity, McLellan and Skinner (1985) concluded that GET and RCP should not be ignored for effective exercise prescription. In another study, Coyle et al. (1988) demonstrated a large-inter individual variability in TTE and [La^-] when exercise was prescribed at 88%$\dot{V}O_{2max}$ to well-trained cyclists homogenous for $\dot{V}O_{2max}$ but differing in lactate threshold (as a %$\dot{V}O_{2max}$). Not only the study of Coyle et al. (1988) provided evidence for the role of lactate threshold as a performance determinant, it also suggested that the intensity-duration relationship could be better described by considering the %$\dot{V}O_{2max}$ at which lactate threshold occurs.

Table 2.2 – The different exercise intensity expressions investigated by McLellan and Skinner (1985).

Method	Intensity Expression	Calculation
1	%$\dot{V}O_{2max}$	$\dot{V}O_{2exercise}$ / $\dot{V}O_{2max}$ × 100
2	%Δ ($\dot{V}O_{2max}$ - GET)	($\dot{V}O_{2exercise}$ - $\dot{V}O_{2GET}$) / ($\dot{V}O_{2max}$ - $\dot{V}O_{2GET}$) × 100
3	%Δ (RCP - GET)	($\dot{V}O_{2exercise}$ - $\dot{V}O_{2GET}$) / ($\dot{V}O_{2RCP}$ - $\dot{V}O_{2GET}$) × 100 ==> if $\dot{V}O_{2GET} \leq \dot{V}O_{2exercise} \leq \dot{V}O_{2RCP}$
	%Δ ($\dot{V}O_{2max}$ - RCP)	($\dot{V}O_{2exercise}$ - $\dot{V}O_{2RCP}$) / ($\dot{V}O_{2max}$ - $\dot{V}O_{2RCP}$) × 100 ==> if $\dot{V}O_{2RCP} < \dot{V}O_{2exercise} \leq \dot{V}O_{2max}$

$\dot{V}O_{2max}$, maximal oxygen uptake; GET, gas exchange threshold; RCP, respiratory compensation point, $\dot{V}O_{2exercise}$, oxygen uptake associated with exercise; $\dot{V}O_{2GET}$, oxygen uptake associated with GET; $\dot{V}O_{2RCP}$, oxygen uptake associated with RCP.

However, McLellan and Gass (1989) later published results that challenged the assumption that combining GET/lactate threshold with $\dot{V}O_{2max}$ would effectively normalise the expression of intensity. Trained cyclists, split into two groups based upon the %$\dot{V}O_{2max}$ at which the lactate threshold occurred, performed 20 min of continuous exercise at the lactate threshold intensity, the lactate threshold plus 33% of the difference between $\dot{V}O_{2max}$ and the lactate threshold (33%Δ), and the lactate threshold plus 67% of the difference between $\dot{V}O_{2max}$ and the lactate threshold (67%Δ). At the lactate threshold, only $\dot{V}O_2$ (by design), ventilation ($\dot{V}E$), and $\dot{V}CO_2$ were significantly different between groups. At 33%Δ, also [La^-] reached significance. However, at 67%Δ, there were between-group differences of large magnitude for most variables, including blood metabolites and acid-base balance in addition to respiratory parameters. Accordingly, these data were interpreted by McLellan and Gass (1989) as evidence "that the lactate threshold and $\dot{V}O_{2max}$ do not represent common

reference points for calculating exercise intensity and/or that another metabolic rate above the lactate threshold and below $\dot{V}O_{2max}$ exists for each individual that defines a maximal cardiorespiratory and metabolic steady state of exercise". Although the combination of GET/lactate threshold with $\dot{V}O_{2max}$ may decrease inter-individual variability in performance, physiological, and perceptual responses to exercise compared with $\%\dot{V}O_{2max}$ only (Lansley et al., 2011, McLellan and Skinner, 1985), it is possible that the use of other benchmarks provides even better results.

Perhaps, for this reason, McLellan and Jacobs (1991) investigated whether the intensity associated with a fixed [La^-] of 4 $mmol \cdot L^{-1}$, which is usually linked with the transition between the heavy and very heavy intensity domains (Faude et al., 2009, Jamnick et al., 2020), could be used to better normalise the rates of muscle glycogen utilisation and [La^-] compared with $\%\dot{V}O_{2max}$. Participants cycled for 30 min at different intensities ranging from 50% to 80%$\dot{V}O_{2max}$. The rationale for this study originated from previous investigations demonstrating that glycogen utilisation was generally related to exercise intensity expressed as $\%\dot{V}O_{2max}$ (Gollnick et al., 1974, Vøllestad and Blom, 1985). Although inter-individual differences in glycogen utilization were neither predicted by $\%\dot{V}O_{2max}$ nor percentage of the power output associated with 4 $mmol \cdot L^{-1}$, [La^-] responses varied less between individuals when the latter expression of intensity was adopted, suggesting some merit in the 4 $mmol \cdot L^{-1}$-based approach (McLellan and Jacobs, 1991).

Given that both the maximal lactate steady state and CP are more robust indicators of the heavy-to-very heavy domain transition compared with a fixed [La^-] (Billat et al., 2003, Faude et al., 2009, Jones et al., 2019), it is likely that using these markers to express intensity would be more effective compared with the power output associated with 4 $mmol \cdot L^{-1}$ as employed by McLellan and Jacobs (1991). More studies are nevertheless necessary to confirm this hypothesis. First, because the applicability of the CP model is restricted to short durations, which may limit its utility (see Section 2.5.1 – Performance-based methods). Second, because the maximal lactate steady state may not necessarily represent the highest intensity at which all physiological and metabolic responses are at steady state (Baron et al., 2003, Hill et al., 2021, Iannetta et al., 2018), raising questions over its basic tenets and suitability for exercise intensity normalisation. Theoretical considerations aside, Faude et al. (2017) have reported inter-individual CVs of around 30% for TTE, 25% for [La^-], and 15% for $\dot{V}E$ and respiratory frequency (f_R) when exercise was performed at the maximal lactate

steady state intensity. These numbers are certainly small compared with the CVs for TTE and [La^-] that are typically obtained when exercise is prescribed on the basis of %$\dot{V}O_{2max}$ (i.e. often > 40%) (Baldwin et al., 2000, Coyle et al., 1988, Gass et al., 1991, Lansley et al., 2011, McLellan and Skinner, 1985, Scharhag-Rosenberger et al., 2010). A study in which exercise responses are modelled according with different intensity expressions is therefore warranted to allow for a fair between-method comparison.

2.5.3 – HIIT methods

The research on exercise intensity prescription methods reviewed in the sections above concerns exercise performed continuously at fixed work rates. However, there are extra challenges for the prescription of HIIT. Cardiorespiratory and metabolic responses to HIIT do not achieve steady state, increasing (or decreasing) continuously within and between work intervals until a peak (or nadir) is attained and exhaustion ensues (Chidnok et al., 2013b, Davies et al., 2017, Rossiter, 2011). It is therefore not possible to factually associate the magnitude of a given physiological response with a particular work rate. In addition, HIIT typically involves multiple abrupt changes in work rate (e.g. 350-W work intervals interspersed with 50-W recovery intervals). As inter-individual differences in $\dot{V}O_2$ kinetic responses to work rate increments and decrements have been observed (Billat et al., 2002, Caputo et al., 2003, Dupont et al., 2010, Ingham et al., 2007), with a potential impact on exercise tolerance (Burnley, 2007, Dupont et al., 2010, Jones and Burnley, 2009), it may be suggested that methods used for the prescription of continuous exercise would not apply to the prescription of HIIT. Yet, this evidence has most frequently been ignored (Bonafiglia et al., 2016, Del Giudice et al., 2020, Maturana et al., 2021, Williams et al., 2019).

Despite the potential challenges inherent to the prescription of HIIT, few studies have been conducted specifically to inform how intensity should be normalised for this type of training (Ferguson et al., 2013, Julio et al., 2020, Nicolò et al., 2014). Interestingly, some derivatives of the CP model have been put forward to explain when exhaustion occurs, either during HIIT (Morton and Billat, 2004, Skiba et al., 2012, Skiba et al., 2015) or field-based high-intensity cycling (Skiba et al., 2014), as thoroughly reviewed by Jones and Vanhatalo (2017). If robust, these models could be used for HIIT prescription as typically done for continuous exercise (see Section 2.5.1 – Performance-based methods). However, not all studies attest to the validity of the CP paradigm when it comes to HIIT (Bartram et al., 2018, Galbraith et al., 2015). Galbraith et al. (2015) recruited 13 distance runners to perform 3 HIIT sessions

with the following patterns: 1000 m at 107%CS interspersed with 200 m at 95%CS, 600 m at 110%CS interspersed with 200 m at 90%CS, and 200 m at 150%CS interspersed with 200 m at 80%CS. Predicted TTEs based upon the model of Morton and Billat (2004) deviated substantially from actual times, with correlation coefficients ranging from -0.21 to -0.04. In another study with 4 elite cyclists, Bartram et al. (2018) tested the model of Skiba et al. (2015) by requesting participants to perform several intermittent bouts involving two 30-s work intervals and a third work interval that was continued until exhaustion. Work intervals were always performed at the work rate predicted to deplete 30% of W', whereas the 60-s recovery intervals were performed at different power outputs, ranging from CP to 200 W below CP. As the individual time constants representing the recovering rate of W' were shown to be higher than those predicted by the model of Skiba et al. (2015), Bartram et al. (2018) concluded that recovery from high-intensity efforts is optimised in elite athletes compared with less trained individuals. Indeed, this notion is consistent with the inter-individual variability observed for the recovery kinetics of muscle $\dot{V}O_2$ (Brizendine et al., 2013, Fennell and Hopker, 2021) and [La^-] (McLellan and Skinner, 1982). How to factor in these inter-individual differences in recovery rate is presently a challenge for scientists and practitioners prescribing HIIT.

While the studies of Galbraith et al. (2015) and Bartram et al. (2018) suggest that individual TTEs during HIIT may be difficult to predict, the results Ferguson et al. (2013) may point in the opposite direction. They asked 8 men to perform three HIIT sessions to exhaustion, all with 4-min work and recovery intervals, at running speeds predicted to expend 100% of D' in 4, 6, and 8 min. As expected, mean TTEs increased with the decrease in running speed, and both peak $\dot{V}O_2$ and peak HR were similar between conditions. Less foreseeable was perhaps that, for all three conditions, inter-individual CVs for TTE reached around 20% only. Although this magnitude of variability may be considered small or large depending on the precision requirements of a given intervention, it is much lower than typically observed for continuous exercise prescribed as $\%\dot{V}O_{2max}$, in which CVs often surpass 40% (Coyle et al., 1988, Lansley et al., 2011, McLellan and Skinner, 1985, Scharhag-Rosenberger et al., 2010). Thus, researchers should be encouraged to attempt replication of the findings of Ferguson et al. (2013) in order to elucidate whether the CP model can be used to effectively normalise the intensity of HIIT.

As is the case with continuous exercise (see Section 2.5.1 – Performance-based methods), it is possible to normalise the intensity of HIIT by taking into account the peak power output (or speed) in combination with the power output (or speed) associated with a predictor of aerobic exercise capacity. For example, Julio et al. (2020) recruited 11 long-distance runners and 10 rugby players to perform three HIIT sessions (15-s work and recovery intervals) with the purpose of quantifying the inter-individual variability in TTE and [La^-] changes from rest associated with different expressions of intensity. Specifically, HIIT sessions were normalised as 110%$\dot{W}_{max}$, $\dot{W}_{max}$ plus 25% of the difference between peak speed and $\dot{W}_{max}$ ($\dot{W}_{max}$+25%$_{PS\text{-}\dot{W}max}$), and $\dot{W}_{max}$ plus 50% of the difference between peak speed and $\dot{W}_{max}$ ($\dot{W}_{max}$+50%$_{PS\text{-}\dot{W}max}$). The inter-individual CV for TTE reduced from 45.2% when work intervals were performed at 110%$\dot{W}_{max}$ to approximately 20% when peak speed was considered for the expression of intensity (i.e. $\dot{W}_{max}$+25%$_{PS\text{-}\dot{W}max}$ and $\dot{W}_{max}$+50%$_{PS\text{-}\dot{W}max}$). Similar reductions in the CV were also observed for [La^-] changes. It must be acknowledged, however, that conditions were not matched for mean intensity, which led to differences in mean TTE. While this is a potential limitation of the work of Julio et al. (2020), it is unlikely that the CVs of approximately 20% associated with both $\dot{W}_{max}$+25%$_{PS\text{-}\dot{W}max}$ and $\dot{W}_{max}$+50%$_{PS\text{-}\dot{W}max}$ would have increased to approximately 45% had conditions been matched.

Perhaps to avoid the issue of intensity normalisation altogether, HIIT has also been prescribed as self-paced exercise in both cross-sectional investigations (Brosnan et al., 2000, Nicolò et al., 2014, Villerius et al., 2008) and training studies (Rønnestad et al., 2020, Seiler et al., 2013, Seiler and Sylta, 2017). This approach assumes that for each HIIT format, reflecting the number of work and recovery intervals and their durations, there exists a maximal sustainable work rate compatible with an individual's physiological capacity (Nicolò et al., 2014, Nicolò and Girardi, 2016). While this assumption can be rationalised in light of the CP model (Jones and Vanhatalo, 2017), it is conceivable that performance during HIIT is more complex than implied by a two-parameter model. Accordingly, prescribing HIIT as self-paced exercise represents a practical alternative for the normalisation of exercise intensity. The main drawbacks of this approach are the requirement for a maximal effort in every session, which is highly dependent on motivation (Wilmore, 1968), and the impact that pacing within and between work intervals may have upon physiological responses to HIIT (Beltrami et al., 2021, Ferguson et al., 2013, Zadow et al., 2015). These can be circumvented by taking the mean work rate across all work intervals and setting HIIT

intensity relative to that value. However, this approach assumes that self- and ergometer-paced performances are equivalent when the mean work rate is identical, which may not be universally true (Black et al., 2015, Thomas et al., 2013). While effective in theory, it has yet to be determined whether the intensity of HIIT can be normalised by means of self-paced exercise purely or as a set percentage of maximal self-paced performance.

2.6 – Summary

The present literature review has identified several key areas in which the evidence is contradictory and/or limited to a few studies. The level of evidence for each topic covered is summarised hereafter. The physiological determinants of endurance performance have been established decades ago, and this topic seems to be relatively well resolved. Also how training should be regulated to optimise physiological capacity ($\dot{V}O_{2max}$ in particular) has long been investigated. However, perhaps because training programmes can be designed in so many ways, the evidence about training regulation is often contradictory. Besides, few training studies have focused on performance, and it is generally assumed (mistakenly) that gains in physiological capacity always translate into performance enhancements. Accordingly, training guidelines are more often established based on general principles as opposed to quantitative models. As for the determinants of adaptive variability in response to training, most of the current understanding derives from the large HERITAGE family study. However, the need to provide a homogenous training stimulus across participants has been overlooked in this and other smaller studies, which may be seen as a major methodological flaw. Although researchers are likely aware of the limitations of their training prescription methods, the lack of studies comparing different approaches for exercise intensity normalisation contributes to the maintenance of the status quo. Indeed, there is no consensus as to the best expression of exercise intensity. In particular, the methods of intensity normalisation for HIIT have received little to no research attention, despite the popularity of this type of training and the prescription challenges associated with non-steady-state exercise.

2.7 – Thesis aims and hypotheses

The overall aim of this thesis was to develop approaches to optimise exercise intensity prescription to enhance the magnitude of the training stimulus and to reduce adaptative variability following HIIT. In particular, the reliability of acute training responses during HIIT was investigated (Chapter 4), the validity of several methods frequently used to

normalise exercise intensity for the prescription of HIIT was assessed (Chapter 5), and two alternative approaches to prescribe HIIT were developed (Chapters 6 and 7). The specific aims of each experimental chapter contributed together to the overall aim of the thesis. These were organised as follows:

Chapter 4 – The aim of this experimental chapter was to assess the consistency with which a certain training stimulus can be achieved from both inter- and intra-individual points of view. Performance, physiological, and perceptual responses of cyclists were quantified as they performed identical HIIT sessions in which exercise intensity was normalised as %Δ. It was hypothesised that low levels of inter- and intra-individual variability would be found for most dependent variables.

Chapter 5 – The aim of this experimental chapter was to compare different methods of intensity normalisation, namely %Δ, %$\dot{W}_{max}$, percentage of the average work rate sustained in a 20-min time-trial, and percentage of W' expenditure, for their ability to normalise acute HIIT responses (i.e. performance, physiological, and perceptual) between individuals. It was hypothesised that at least one method would elicit markedly lower inter-individual variability in acute HIIT responses.

Chapter 6 – The aim of this experimental chapter was to compare the physiological and perceptual responses elicited by work intervals matched for duration and mean power output but differing in power output distribution. Specifically, constant-intensity work intervals were prescribed in one of the HIIT sessions, whereas power output was repeatedly varied within the work intervals of the other. It was hypothesised that higher %$\dot{V}O_{2max}$ would be sustained in the varied-intensity mode.

Chapter 7 – The aim of this experimental chapter was to assess the inter-individual variability in acute and adaptive responses to a training programme in two groups of cyclists. It was hypothesised that the group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session would exhibit lower inter-individual variability in acute exercise responses, leading to lower variability in adaptive responses, in comparison with the group in which training intensity was prescribed as %$\dot{W}_{max}$. It was also hypothesised that the mean group (adaptive) responses would be compromised in the group with larger inter-individual variability, owing to a higher

proportion of unfinished training sessions due to premature exhaustion (i.e. large inter-individual performance variability).

Chapter 3 – General methods

3.1 – Aim

The aim of this chapter is to describe common methodological approaches and calibration routines between experimental Chapters 4, 5 and 7 of this thesis. While experimental procedures described in these chapters were performed at the same laboratory with the same equipment (School of Sport and Exercise Sciences, University of Kent, Chatham, UK), experimental procedures described in chapter 6 were performed elsewhere (Section for Health and Exercise Physiology, Inland Norway University of Applied Sciences, Lillehammer, Norway). Accordingly, the reader is referred to chapter 6 for its detailed methodological approach and calibration routines.

3.2 – General standards

The institution's ethics committee approved each study in compliance with the Declaration of Helsinki, except for pre-registration in a public database, and all participants provided written informed consent. Prior to the first laboratory visit of each study, participants received standard instructions, which were valid for all visits, except for the visits of the training intervention detailed in Chapter 7. They were requested to refrain from all types of intense exercise 48 h before each laboratory visit and to prepare as they would for competition. They were also requested to standardise meals 24 h before each visit, and either record them on a food diary to enhance compliance (Chapter 5) or consume the last large meal at least 2 h before arriving at the laboratory (Chapter 7). The consumption of caffeine was not allowed in the last 24 h before testing (last 12 h for Chapter 7). All tests were performed free from distractions, under similar environmental conditions (16-17°C), with participants being cooled with a fan. Maximal encouragement was always provided to warrant representative performances.

3.3 – Testing standards

Participants' body mass (760 scale, Seca, Hamburg, Germany) and height (213 stadiometer, Seca, Hamburg, Germany) were measured to the nearest 0.1 kg and 0.5 cm, respectively. Study participants were cyclists, and they used their own bikes mounted on a cycle ergometer (Cyclus 2, RBM Elektronik-Automation, Leipzig, Germany). For the incremental tests and HIIT sessions, the ergometer was set at power mode (i.e. cadence independent). For the 3-min all-out tests (Chapter 5), the 20-min time-trials (Chapter 5), and the self-paced interval training sessions (Chapter 7), the ergometer was set at inclination mode (i.e. 0%; cadence dependent), and participants were required to change gears, as if they were riding outdoors.

HR was continuously monitored during all sessions through an ANT+ belt transmitter (Cyclus 2, RBM Elektronik-Automation, Leipzig, Germany). Power output, HR, elapsed time and cadence were visible, except for the 3-min all-out tests (Chapter 5; all concealed) and HIIT sessions (Chapter 5; power output and HR concealed).

Incremental tests were preceded by a 10-min warm-up at 100 W for men, and 50 W for women. Work rate increased continuously at 25 $W \cdot min^{-1}$ until voluntary exhaustion, or participants' inability to maintain cadence above 70 $rev \cdot min^{-1}$. HIIT sessions were preceded by different warm-ups in each study (the reader is referred to individual chapters for a detailed description), but the workout format was always the same (i.e. 4-min work intervals interspersed with 2-min active recovery). When HIIT sessions were performed to exhaustion (Chapters 4 and 5), the same criteria of the incremental test were adopted to determine the end of the session. When participants were able to complete ten work intervals, HIIT sessions were terminated, although participants were not aware of this arbitrary endpoint.

Breath-by-breath gas exchange was continuously monitored through a metabolic cart (MetaLyzer 3B, Cortex Biophysik, Leipzig, Germany) during the incremental test and HIIT sessions (except for the training intervention in Chapter 7). Calibration was performed according to the manufacturer's instructions prior to every test, even when participants performed more than one test per laboratory visit. A two-point gas calibration was achieved using ambient air and a certified (i.e. alpha standard) compressed gas mix of 17.29% O_2 and 5.18% CO_2 with a balance of N_2 (BOC, Guildford, UK). The flow sensor and turbine were calibrated using a 3-L syringe (Hans Rudolph, Shawnee, USA) moved in time with a set flow rate.

Several measures were obtained during the incremental test. $\dot{V}O_{2max}$ was identified as the highest 30-s mean $\dot{V}O_2$ (60-s mean for Chapter 7), and $\dot{W}_{max}$ as the mean power output of the last minute. GET was obtained according with the procedures described by Lansley et al. (2011), as the first disproportionate increase in $\dot{V}CO_2$ versus $\dot{V}O_2$; an increase in ventilatory equivalent for oxygen with no increase in ventilatory equivalent for carbon dioxide; and an increase in end-tidal oxygen tension with no fall in end-tidal carbon dioxide tension. Two-thirds of the ramp rate was deducted from the work rate at GET to account for the $\dot{V}O_2$ mean response time. HR_{max} was identified as the highest value recorded.

Immediately after the incremental test, a blood sample was taken to establish peak [La^-], and peak RPE was noted.

During HIIT, RPE was indicated immediately after each work interval and at exhaustion. Blood samples for the assessment of [La^-] were collected 20 s into the recovery interval, and 20 s after exhaustion (Chapters 4 and 5). In the last 30 s of each warm-up and cool-down bouts, participants indicated their RPE, and a blood sample was collected for [La^-] assessment (Chapters 4 and 5).

RPE was assessed during exercise based on the 6-20 Borg's scale (Borg, 1982). Session RPE (sRPE) was recorded 10 min after the cool-down that followed HIIT sessions, in which participants were asked "How was your workout?" based on the modified 0-10 scale (Foster et al., 2001) (Chapters 4 and 5). Standard written instructions were provided, and RPE was defined as "the conscious sensation of how hard, heavy, and strenuous a physical task is" (Marcora, 2010).

Fingertip capillary blood samples, collected in 10 µL heparinised glass tubes (Paul Marienfeld, Lauda-Königshofen, Germany), were assessed for [La^-] by an automatic analyser (Biosen C-Line, EKF Diagnostics, Penarth, UK) immediately after acquisition. The analyser was calibrated using the manufacturer's recommended 12 $mmol \cdot L^{-1}$ standard (EKF Diagnostics, Penarth, UK) prior to the first use on a given day, and every 60 min afterwards.

Changes from a 3-min resting baseline (arbitrarily set to zero) in muscle tissue oxygen saturation (ΔStO_2) and concentration of deoxygenated heme compounds (Δdeoxy[heme]) were assessed during the HIIT sessions of Chapter 5 using continuous-wave near-infrared spectroscopy (Portamon, Artinis Medical Systems, Elst, Netherlands) at a sampling rate of 10 Hz. The near-infrared spectroscopy signal for deoxygenated haemoglobin and myoglobin was multiplied by four to express data as units of heme (Barstow, 2019). The inter-optode distance was 35 mm and a differential path-length factor of 4.0 was assumed for all tests. The device was placed on the vastus lateralis above the upper patella border, at one-third of the distance between the patella and greater trochanter, parallel to the longitudinal femur axis. This site was shaved, and adipose tissue thickness was estimated by skinfold callipers as the halved median of three measurements (3.6 ± 2.3 mm) (Barstow, 2019). Motion artefacts were minimised by fixating the device position using a cohesive compression

bandage. Plastic wrap and a light-absorbing black cloth were used to cover the apparatus. Position was marked for replication in subsequent measurements.

3.4 – Questionnaires

This section refers to Chapters 4 and 5 only. Upon arrival at the laboratory, participants answered a series of questions to determine their cycling experience (Edwards et al., 2009) (first visit only), intrinsic and success motivations (Matthews et al., 2001), and sports emotions (i.e. anxiety, dejection, excitement, anger, and happiness) (Jones et al., 2005). They also indicated their sleep duration, and rated from 1 to 10 their sleep quality, motivation to train, appetite, overall recovery status, muscle soreness, how heavy they were feeling, and how heavy their legs were feeling. These latter scales were adapted from a previous version of the Norwegian Olympic Committee's training diary (http://olt-dagbok.nif.no) and are hereafter referred to as training diary scales. At the end of each exercise session, participants rated subjective workload using the National Aeronautics and Space Administration Task Load Index (NASA-TLX) composed of six subscales: mental demand, physical demand, temporal demand, performance, effort, and frustration (Hart, 2006). In the morning after each laboratory visit, participants indicated their sleep duration and completed the training diary scales once more (Chapter 5 only). Questionnaires and scales were administered in the first visit of each study for familiarization purposes only.

Chapter 4 – The delta concept is not a valid method to normalise the intensity of exhaustive interval training

4.1 – Introduction

It has been suggested that improvements in physical performance are driven by repeated exposure to the metabolic strain associated with each session of a training programme (Hawley et al., 2014). Therefore, training must be carefully prescribed to provide an optimal stimulus for adaptation. As the magnitude of several responses to exercise is intensity-dependent (Barstow et al., 1993, Gollnick et al., 1974, Hill et al., 2008, Nordsborg et al., 2010), work rate choice may play a critical role in the regulation of adaptive processes (Granata et al., 2018, MacInnis and Gibala, 2017). Even though this is a simple concept to understand, it is not as easily implemented. For example, if a standard work rate (e.g. 200 W) is prescribed to a group of people, factors such as training status, body dimensions and sex will affect how each person responds. The effective expression of exercise intensity thus depends on an individual's physiological capacity (i.e. relative intensity). While this issue has been long recognised (Gleser and Vogel, 1973), debate persists as to the best method to normalise exercise intensity prescription (Jamnick et al., 2020, Mann et al., 2013).

Traditionally, exercise intensity is often normalised as $\%\dot{V}O_{2max}$ (e.g. Åstrand and Ryhming (1954)). This approach has nevertheless been criticised for eliciting inconsistent physiological responses between individuals when used for exercise prescription (Coyle et al., 1988, Egger et al., 2016, Jamnick et al., 2020, Lansley et al., 2011, Mann et al., 2013, Scharhag-Rosenberger et al., 2010). Essentially, $\%\dot{V}O_{2max}$ does not take into account the metabolic thresholds governing gas exchange, blood acid-base, and intramuscular responses to exercise (Iannetta et al., 2020, Jamnick et al., 2020, Mann et al., 2013). As a consequence, the %Δ method has been proposed for its ability to reduce inter-individual variability in TTE and physiological/perceptual responses compared with $\%\dot{V}O_{2max}$ (Lansley et al., 2011, McLellan and Skinner, 1985):

$$\dot{W}_{target} = \dot{W}_{GET} + [(\dot{W}_{\dot{V}O2max} - \dot{W}_{GET}) \cdot \%\Delta] \quad (4.1)$$

where $\dot{W}_{target}$ is the target work rate, $\dot{W}_{GET}$ is the work rate associated with GET, $\dot{W}_{\dot{V}O2max}$ is the work rate associated with the $\dot{V}O_{2max}$, and %Δ is the relative intensity chosen. Despite the aforementioned reductions in inter-individual variability, %Δ is far from being universally adopted in sport and exercise sciences (Jamnick et al., 2020), suggesting more studies may be required to attest to its efficacy.

Whilst the effectiveness of %Δ has been previously investigated for continuous exercise, it has not been assessed in the context of HIIT. On average, HIIT has been associated with larger improvements in cardiorespiratory fitness than continuous training when energy expenditure is accounted for (Bacon et al., 2013, Maturana et al., 2021, Williams et al., 2019); yet, inter-individual variability in training adaptation seems to be as prevalent for HIIT as it is for continuous training programmes (Coakley and Passfield, 2018b, Maturana et al., 2021, Williams et al., 2019). These observations might indicate that simply increasing exercise intensity to enhance the training stimulus is insufficient to minimise adaptive variability. While cognizant of the role played by genetics (Bouchard et al., 1999, Mann et al., 2014, Sarzynski et al., 2017), it is possible that adaptive variability may be more reflective of a methodological problem. An inconsistent level of homeostatic disturbance between individuals, secondary to an inadequate intensity normalisation strategy, may result in inter-individual variability in training adaptations (Iannetta et al., 2020, Mann et al., 2014). Assessing the utility of %Δ for HIIT prescription is therefore a key step to understanding if a both large and homogeneous training stimulus can be provided to a group.

If a method of intensity normalisation is to be useful, exercise responses ideally need to be reproducible session to session. So far, little attention has been paid to this potential source of variability in the context of training prescription (Chrzanowski-Smith et al., 2020, Egger et al., 2016, Faude et al., 2017, Sarzynski et al., 2017). In a secondary analysis of data from the HERITAGE family study, Sarzynski et al. (2017) investigated whether recorded HR and work rates matched prescribed targets for each training session. Remarkably, session-to-session fluctuations accounted for at least 6% of the inter-individual variability in $\dot{V}O_{2max}$ adaptive responses (Sarzynski et al., 2017), highlighting the importance of ensuring a reproducible training stimulus. Whether the anticipated exercise responses are achieved whenever a HIIT session is performed remains to be investigated.

The aim of this study was to quantify inter- and intra-individual variability in performance, physiological, and perceptual responses of cyclists performing identical HIIT sessions with intensity prescribed based on %Δ. It was assumed that these variability estimates would represent the consistency with which a certain training stimulus can be achieved. Based on previous findings (Lansley et al., 2011, McLellan and Skinner, 1985), low levels of inter- and intra-individual variability in most dependent variables were hypothesised.

4.2 – Methods

4.2.1 – Participants

Eighteen male and four female recreationally trained cyclists volunteered for this study (age: 36 ± 12 years, height: 178 ± 10 cm, body mass: 75.2 ± 13.7 kg, cycling experience index: 24 ± 7 (see Edwards et al. (2009) for details)). Ethical standards compliance is detailed in Chapter 3 – General methods.

4.2.2 – Study design

Participants attended the laboratory on five occasions, at the same time of the day, separated by at least 48 h. In the first visit, they completed an incremental test to exhaustion (see Chapter 3 – General methods for details). In each of the next four visits, identical HIIT sessions were performed to exhaustion (see Chapter 3 – General methods for details). Performance, physiological, and perceptual responses were quantified and modelled to provide estimates of inter- and intra-individual variability.

4.2.3 – HIIT sessions

Common procedures and questionnaires are outlined in Chapter 3 – General methods. The warm-up involved three 7-min bouts consecutively at 60%, 70%, and 80% of $\dot{W}_{GET}$. The first work interval started 2 min after the warm-up was terminated. The work rate of the work intervals ($\dot{W}_{target}$) was calculated via equation 4.1, based on the relative intensity of 70%Δ. Recovery intervals were performed at 20%$\dot{W}_{target}$. In the last 10 s before HIIT sessions started, participants increased cadence to >100 rev·min^{-1}, but cadence was self-selected afterwards, during both work and recovery intervals. After participants reached exhaustion, a 3-min rest was allowed, and a cool-down identical to the warm-up was performed.

4.2.4 – Data processing

Raw breath-by-breath gas data were smoothed to 5-s averages. Time at >90%$\dot{V}O_{2max}$ and time at >95%$\dot{V}O_{2max}$ were calculated for each HIIT session by summing all $\dot{V}O_2$ samples above the established cut-off. Time at >90%$\dot{V}O_{2max}$ and time at >95%$\dot{V}O_{2max}$ were also calculated as %TTE. Cadence was analysed as the average of each work interval. Relative $\dot{V}O_2$, HR, $\dot{V}E$, and f_R were analysed as the average of the last minute of each work interval, or the completed duration if shorter than one minute (although maximal responses were sometimes elicited during the last complete work interval, but not during the incomplete one).

4.2.5 – Data analysis

Data were assessed for normality using Shapiro-Wilk's test and normal quantile plots, with subsequent analysis chosen accordingly. One-way repeated measures analysis of variance was performed to test for systematic changes between HIIT sessions, with Bonferroni pairwise comparisons being used to identify where significant differences existed within the data. To calculate inter- and intra-individual variability components for the repeated HIIT sessions, a linear mixed model was fitted to the dependent variables with participant as a random effect. Inter- and intra-individual variability are reported as SD (absolute) or percentage (relative). Ninety-five percent confidence limits were calculated by bootstrap sampling based on 200 repetitions. When appropriate, work interval was considered as a covariate, as well as linear, quadratic or cubic terms. The best model was selected based on the Akaike information criterion. Systematic changes between HIIT sessions were assessed using Prism 8 (GraphPad, San Diego, USA) and data modelling was performed using R 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria). Significance level was set at $P \leq 0.05$. Results are presented as mean ± SD, unless otherwise stated. To aid understanding of results, the reader unfamiliarised with linear mixed models is referred to Brown (2021) for a tutorial.

4.3 – Results

During the incremental test, participants attained a $\dot{V}O_{2max}$ of 51.6 ± 5.3 $ml \cdot kg^{-1} \cdot min^{-1}$, $\dot{W}_{max}$ of 4.72 ± 0.48 $W \cdot kg^{-1}$, peak HR of 179 ± 14 $beats \cdot min^{-1}$, peak respiratory exchange ratio of 1.16 ± 0.10, $[La^{-}]$ of 11.9 ± 2.3 $mmol \cdot L^{-1}$, and RPE of 19.0 ± 0.9. The work and recovery intervals of the HIIT sessions were performed at 4.00 ± 0.43 $W \cdot kg^{-1}$ (85 ± 3 $\%\dot{W}_{max}$) and 0.80 ± 0.09 $W \cdot kg^{-1}$ (17 ± 1 $\%\dot{W}_{max}$), respectively.

No systematic changes over repeated HIIT sessions were evident for TTE ($F = 2.10$, $P = 0.13$, $\eta_p^2 = 0.09$), time at >90%$\dot{V}O_{2max}$ ($F = 2.08$, $P = 0.12$, $\eta_p^2 = 0.09$), sRPE ($F = 0.16$, $P = 0.84$, $\eta_p^2 = 0.01$), intrinsic motivation ($F = 2.57$, $P = 0.08$, $\eta_p^2 = 0.11$), success motivation ($F = 0.79$, $P = 0.46$, $\eta_p^2 = 0.04$), dejection ($F = 0.88$, $P = 0.43$, $\eta_p^2 = 0.04$), anger ($F = 0.74$, $P = 0.48$, $\eta_p^2 = 0.03$), sleep duration ($F = 2.15$, $P = 0.12$, $\eta p2 = 0.09$), or any of the training diary scales (all $F \leq 2.04$, $P \geq 0.13$, $\eta_p^2 \leq 0.09$) and NASA-TLX subscales (all $F \leq 2.34$, $P \geq 0.10$, $\eta_p^2 \leq 0.10$).

However, there was a between-HIIT session effect for time at >95%$\dot{V}O_{2max}$ (F = 3.55, P = 0.027, η_p^2 = 0.14), anxiety (F = 4.29, P = 0.010, η_p^2 = 0.17), excitement (F = 4.72, P = 0.006, η_p^2 = 0.18), and happiness (F = 3.26, P = 0.039, η_p^2 = 0.13). Bonferroni pairwise comparisons revealed that time at >95%$\dot{V}O_{2max}$ was higher in session 4 compared with 1 (P = 0.022), anxiety was lower in session 4 compared with 2 (P = 0.040), and both excitement and happiness were lower in session 3 compared with 1 (both P ≤ 0.012).

Inter- and intra-individual variability components of performance, physiological, and perceptual responses to HIIT are presented in Table 4.1. Models are illustrated in Figure 4.1.

Table 4.1 – Linear mixed model estimates [95% confidence limits].

Dependent Variable	Best Model	Intercept	Inter-individual SD	Intra-individual SD	Inter-individual variability (%)	Intra-individual variability (%)
TTE (min)	Random identity effect	20.3 [15.9 – 24.2]	9.3 [6.4 – 12.2]	4.5 [3.7 – 5.2]	81.2 [65.2 – 89.3]	18.8 [10.6 – 32.8]
Cadence ($rev \cdot min^{-1}$)	Linear term for work interval, random identity effect	97 [94 – 100]	7 [4 – 9]	4 [4 – 4]	71.7 [53.1 – 81.5]	28.3 [17.6 – 46.8]
Oxygen Uptake ($ml \cdot kg^{-1} \cdot min^{-1}$)	Linear term for work interval, random identity effect	49.9 [48.0 – 51.7]	4.6 [3.1 – 6.3]	2.4 [2.2 – 2.7]	77.9 [62.2 – 86.4]	22.1 [13.5 – 35.5]
RPE	Quadratic term for work interval, random identity effect	14.5 [13.8 – 15.2]	1.6 [1.2 – 2.1]	1.0 [0.9 – 1.0]	72.9 [56.4 – 82.8]	27.1 [17.1 – 41.1]
$[La^{-}]$ ($mmol \cdot L^{-1}$)	Cubic term for work interval, random identity effect	4.3 [3.1 – 5.5]	2.0 [1.4 – 2.5]	1.6 [1.4 – 1.7]	61.1 [44.4 – 72.8]	38.9 [27.1 – 55.3]
Heart Rate ($beats \cdot min^{-1}$)	Cubic term for work interval, random identity effect	162 [156 – 167]	12 [8 – 16]	4 [4 – 5]	88.6 [76.4 – 93.1]	11.4 [6.5 – 22.3]
Ventilation ($L \cdot min^{-1}$)	Quadratic term for work interval, random identity effect	128 [116 – 139]	25 [18 – 33]	11 [11 – 12]	83.1 [71.3 – 89.2]	16.9 [10.7 – 28.2]
Respiratory Frequency ($cycles \cdot min^{-1}$)	Quadratic term for work interval, random identity effect	41 [38 – 45]	8 [5 – 10]	4 [4 – 4]	79.0 [62.8 – 86.1]	21.0 [13.3 – 36.3]
Time at >90%$\dot{V}O_{2max}$ (s)	Random identity effect	502 [346 – 652]	337 [238 – 447]	144 [118 – 169]	84.5 [70.8 – 90.9]	15.5 [8.7 – 28.0]
Time at >95%$\dot{V}O_{2max}$ (s)	Random identity effect	320 [218 – 422]	279 [170 – 358]	139 [116 – 162]	80.0 [55.3 – 88.3]	20.0 [11.5 – 42.0]

Time at >90%$\dot{V}O_{2max}$ (%TTE)	Random identity effect	40.8 [35.2 – 46.2]	11.3 [7.2 – 15.6]	11.3 [9.2 – 13.3]	50.0 [25.2 – 70.3]	50.0 [29.3 – 73.8]
Time at >95%$\dot{V}O_{2max}$ (%TTE)	Random identity effect	25.3 [20.0 – 31.5]	12.5 [7.4 – 16.4]	11.5 [9.3 – 13.3]	54.2 [29.1 – 72.9]	45.8 [27.0 – 70.4]
sRPE	Random identity effect	7.8 [7.3 – 8.3]	1.3 [0.8 – 1.7]	0.7 [0.6 – 0.8]	77.0 [51.5 – 86.4]	23.0 [13.3 – 45.0]

SD: standard deviation, RPE: ratings of perceived exertion, [La^-]: blood lactate concentration, $\dot{V}O_{2max}$: maximal oxygen uptake, TTE: time to exhaustion, sRPE: session ratings of perceived exertion.

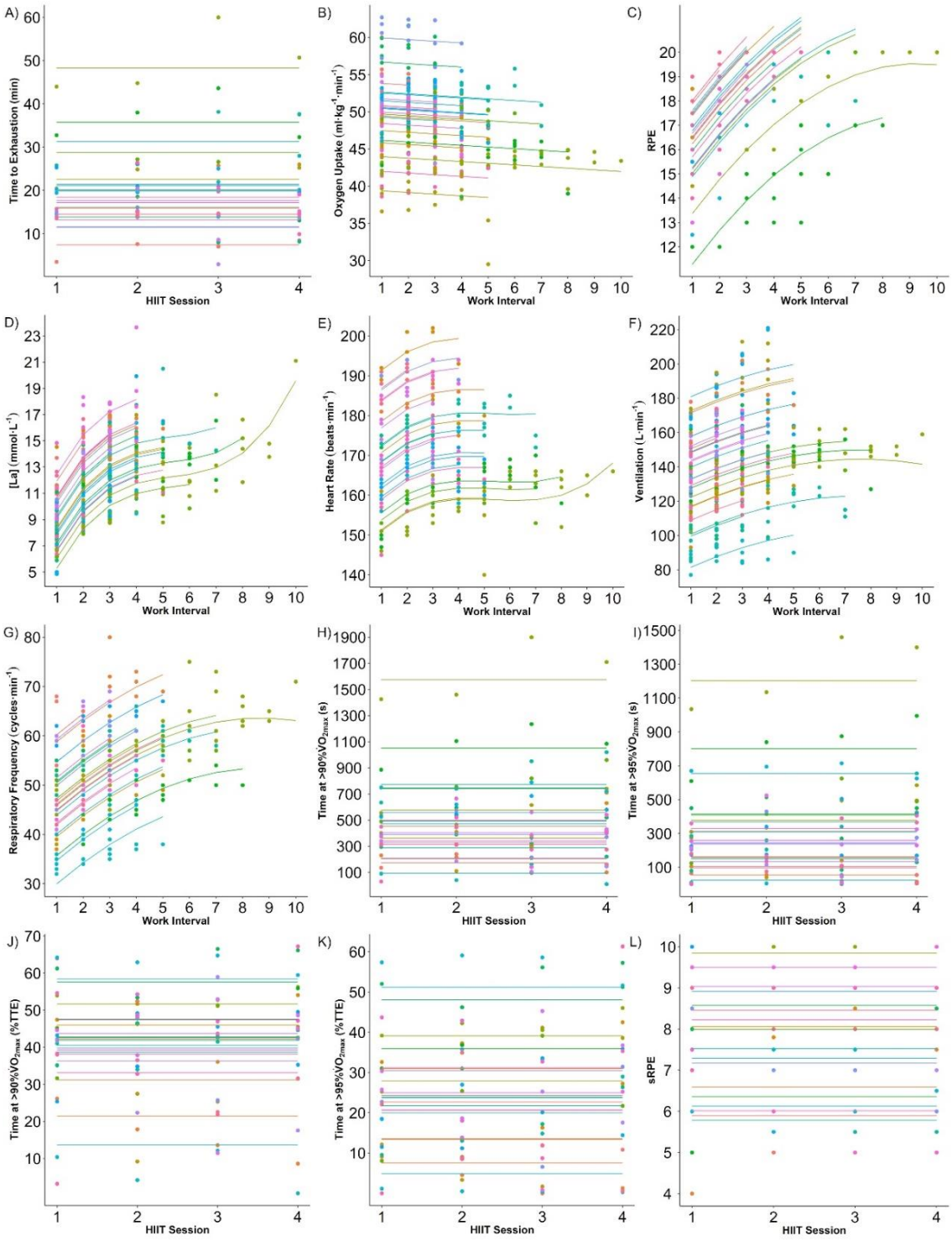

Figure 4.1 – Model illustration for time to exhaustion (panel A), oxygen uptake (panel B), ratings of perceived exertion (RPE, panel C), blood lactate concentration ([La^-], panel D), heart rate (panel E), ventilation (panel F), respiratory frequency (panel G), time above 90% or 95% of maximal oxygen uptake (time at >90%$\dot{V}O_{2max}$/>95%$\dot{V}O_{2max}$, panels H, I, J, and K), and session ratings of perceived exertion (sRPE, panel L). Each colour represents a unique research participant. Dots represent individual measures and lines represent modelled participants' responses.

4.4 – Discussion

This is the first investigation into the effectiveness of %Δ as a method to normalise the intensity of HIIT sessions across individuals. This is also one of the few studies designed to investigate intensity normalisation in which repeated testing was implemented to statistically partition inter- and intra-individual variability (Egger et al., 2016, Faude et al., 2017). Even though %Δ has been advocated in the context of intensity prescription for continuous exercise (Lansley et al., 2011, McLellan and Skinner, 1985), the findings of the present study raise questions regarding its broad-spectrum utility. The levels of inter- and intra-individual variability observed were substantial for most dependent variables, refuting the study hypothesis. Importantly, the larger inter-individual variability, relative to intra-individual variability, suggests that an inadequate normalisation of exercise intensity using this prescription method cannot be attributed to day-to-day biological fluctuations and/or measurement errors.

There is growing consensus that %$\dot{V}O_{2max}$ should not be used for exercise intensity normalisation (Coyle et al., 1988, Egger et al., 2016, Iannetta et al., 2020, Jamnick et al., 2020, Lansley et al., 2011, Mann et al., 2013, Scharhag-Rosenberger et al., 2010). Alternatively, it has been proposed that both $\dot{V}O_{2max}$ and GET are taken into account (i.e. %Δ) for better normalisation of intensity prescription (Lansley et al., 2011, McLellan and Skinner, 1985). McLellan and Skinner (1985) sought to identify the best expression of intensity to predict TTE as their participants exercised continuously at work rates eliciting approximately 75%, 85%, and 95%$\dot{V}O_{2max}$. By modelling the relationship between the logarithm of TTE and intensity, authors reported a larger explained variance (R^2 = 0.88 versus 0.85) and a lower standard error of estimate (SEE = 0.102 [~ 3 min] versus 0.118 [~ 3.4 min]) for %Δ compared with %$\dot{V}O_{2max}$ (McLellan and Skinner, 1985). While %Δ was not compared with any other method in the present study, our results disagree with those of McLellan and Skinner (1985), as TTE associated with HIIT sessions would be more difficult to predict in view of inter- and intra-individual SDs of 9.3 and 4.5 min, respectively. Lansley et al. (2011) investigated the relationship between exercise intensity expression and inter-individual variability in several exercise responses. Relative to the mean TTE (20.3 min), the inter-individual SD for HIIT performed at 70%Δ in the present study (9.3 min or 45.8%) was higher than the SDs reported by Lansley et al. (2011) for continuous exercise at either 80%Δ (8.6 ± 1.8 min or 20.9%) or 90%$\dot{V}O_{2max}$ (5.4 ± 2.3 min or 42.6%). While it may be argued that the aforementioned TTE comparisons are not valid due to differences in study

design, exercise pattern (continuous versus intermittent), and range of exercise intensities tested, also the inter-individual SDs for RPE, [La^-], HR, and $\dot{V}E$ in the present study were similar, if not superior, to those produced by 90%$\dot{V}O_{2max}$ in the study of Lansley et al. (2011). Altogether, it may be concluded that a) individual responses to HIIT are naturally more unpredictable compared with continuous exercise, and/or b) the use of %Δ should not be recommended for HIIT.

One challenge related to the prescription of exercise intensity is that there is little understanding of the reproducibility of performance, physiological, and perceptual responses to each type of exercise used in training programmes (Chrzanowski-Smith et al., 2020, Faude et al., 2017). As these variables reflect the metabolic strain of a training session, which ultimately signals for many adaptive processes (Granata et al., 2018, Hawley et al., 2014, MacInnis and Gibala, 2017), large intra-individual SDs for acute exercise responses could mean that individual adaptive rates are unpredictable on the basis of a given training stimulus. Furthermore, any attempt to reduce inter-individual variability through the optimisation of relative intensity prescription would be pointless. That said, inter- and intra-individual variability averaged across all variables 73.9% and 26.1%, respectively. These numbers suggest that a potential mismatch between intended and observed responses to HIIT would likely reflect a methodological issue in the intensity normalisation, rather than day-to-day biological fluctuations and/or measurement errors.

In absolute terms, however, the intra-individual SD may be considered high for some variables, indicating uncertainty as to how a given individual responds to identical HIIT sessions. For example, the SD for TTE (4.5 min) was greater than the duration of the work intervals (i.e. 4 min). This might indicate that the intensity of fixed-duration HIIT sessions of similar format (i.e. 4-min on, 2-min off) should be conservatively set to allow individuals to complete one or two work intervals more than predicted if all training sessions of a programme are to be finished. Relative to the mean TTE, the intra-individual SD (22.2%) was similar to that reported by Faude et al. (2017) for continuous exercise at the maximal lactate steady state (24.6%), but higher than that reported by Midgley et al. (2007) for running-based HIIT (11.5%). These estimates reflect moderate-to-large levels of uncertainty that must be dealt with whatever the method used for normalisation of relative exercise intensity. As for the physiological and perceptual responses, the intra-individual SDs for $\dot{V}O_2$ (2.4 versus 1.6 $ml \cdot kg^{-1} \cdot min^{-1}$), RPE (1.0 versus 0.4), [La^-] (1.6 versus 0.8 $mmol \cdot L^{-1}$),

$\dot{V}E$ (11 versus 8 $L \cdot min^{-1}$), and f_R (4 versus 2 $cycles \cdot min^{-1}$) were higher than those reported by Faude et al. (2017), but not for HR (4 versus 4 $beats \cdot min^{-1}$). However, these figures might be considered comparable if the higher exercise intensity and associated heightened responses of the present study are taken into account. Of note, it is unclear whether the level of intra-individual variability reported here and elsewhere (Faude et al., 2017) represents biological "noise" or indeed a variable training stimulus following identical exercise sessions. In this respect, time at >90%$\dot{V}O_{2max}$ (SD = 144 s, CV = 28.6%) and time at >95%$\dot{V}O_{2max}$ (SD = 139 s, CV = 43.4%) were poorly reproducible, corroborating the data from Midgley et al. (2007) on running-based HIIT (time at >90%$\dot{V}O_{2max}$ SD = 119 s, CV = 24.5%; and time at >95%$\dot{V}O_{2max}$ SD = 82 s, CV = 34.5%).

While the large estimates of inter-individual variability reported here are specific for prescriptions based on %Δ, there is no reason to believe that traditional (and simpler) methods such as %$\dot{V}O_{2max}$ would elicit HIIT responses much more homogeneous, given the literature on the topic (Coyle et al., 1988, Egger et al., 2016, Iannetta et al., 2020, Jamnick et al., 2020, Lansley et al., 2011, Mann et al., 2013, Scharhag-Rosenberger et al., 2010). Therefore, the present findings are in line with the hypothesis that inter-individual variability in training adaptation, as demonstrated following either HIIT or continuous training programmes (Coakley and Passfield, 2018b, Maturana et al., 2021, Williams et al., 2019), are not primarily attributed to genetics (Joyner, 2019, Marsh et al., 2020). For instance, in the HERITAGE family study, from which heritability estimates of around 50% have been derived for $\dot{V}O_{2max}$ gains with training (Bouchard et al., 1999, Sarzynski et al., 2017), exercise intensity was prescribed based on individual $\dot{V}O_2$-HR relationships, which can be biased by several factors (Gilman, 1996), to target a given %$\dot{V}O_{2max}$. This leaves open the possibility that the role of genetics has consequently been overestimated due to a methodological issue.

This study is not without limitations. Even though effort has been directed to ensure standardised conditions across sessions, a small training effect cannot be discarded, given that time at >95%$\dot{V}O_{2max}$ was higher in session 4 compared with 1. There might have been also a psychological effect manifested as changes in pre-exercise emotions. Anxiety was lower in session 4 compared with 2, and both excitement and happiness were lower in session 3 compared with 1. The extent to which these changes affected the variability estimates is currently unknown.

In summary, the results of this study demonstrate that %Δ does not effectively normalise the relative intensity of HIIT across individuals. The levels of inter- and intra-individual variability observed were substantial for most acute exercise responses. Importantly, inter-individual variability was generally larger relative to intra-individual variability, suggesting that the poor normalisation of exercise intensity produced by %Δ cannot be attributed to day-to-day biological fluctuations and/or measurement errors. Future studies should investigate the validity of alternative methods of intensity prescription for HIIT and the impact of intra-individual variability in acute exercise responses on training adaptations.

Chapter 5 – Current methods to prescribe exercise intensity are inappropriate for exhaustive interval training

5.1 – Introduction

The prescription of endurance training involves decisions about intensity, duration, frequency, and mode of exercise. Of these variables, exercise intensity is generally the most challenging to prescribe. This difficulty stems from the fact that a given work rate may elicit varying levels of cardiorespiratory and metabolic stress depending on the individual's physiological capacity. Therefore, the first step in setting training targets is to decide on a test that provides a prescription benchmark to be used for the normalisation of relative intensity.

In science, an incremental test to exhaustion has typically been the preferred method to measure $\dot{V}O_{2max}$ as an index of cardiorespiratory fitness (Hawkins et al., 2007). Likewise, using fractions of an individual's $\dot{V}O_{2max}$ to express exercise intensity has been a common practice for decades (Åstrand and Ryhming, 1954). However, there are criticisms of this approach. Some studies suggest that using $\%\dot{V}O_{2max}$ to prescribe exercise may elicit highly heterogeneous responses between individuals (e.g. [La^-], RPE, TTE) (Baldwin et al., 2000, Coyle et al., 1988, Egger et al., 2016, Iannetta et al., 2020, Lansley et al., 2011, McLellan and Skinner, 1985, Meyer et al., 1999, Scharhag-Rosenberger et al., 2010). Therefore, the effectiveness of training programmes based upon $\%\dot{V}O_{2max}$ would be likely compromised in those individuals experiencing less homeostatic perturbations given the role of relative exercise intensity in activating signalling pathways that mediate physiological adaptation (Granata et al., 2018, MacInnis and Gibala, 2017). Such a prospect indicates that alternative benchmarks should be considered for exercise intensity normalisation.

In 2013, Mann et al. (2013) reviewed some of the methods to prescribe exercise intensity described in the literature. No consensus emerged as to the best method (Mann et al., 2013), with a similar conclusion being reached by a more recent review (Jamnick et al., 2020). It has been argued that the optimal method of intensity prescription may be context-dependent, as population of interest, targeted intensity domain (i.e. moderate, heavy, very heavy, or severe (Rossiter, 2011)), and exercise pattern (i.e. continuous or intermittent) are likely to determine the ideal choice (Jamnick et al., 2020, Mann et al., 2013). For this reason, it seems counterintuitive that few studies have investigated exercise intensity normalisation for HIIT (Bartram et al., 2018, Ferguson et al., 2013, Galbraith et al., 2015, Julio et al., 2020). In this type of training, exercise is performed intermittently at work rates that can be sustained for only a few minutes, due to the energetic demand exceeding the capacity of muscle cells to

synthesise ATP (Rossiter, 2011). Performance variability at such intensities can be explained by the CP model (Jones and Vanhatalo, 2017), and it is therefore unsurprising that most HIIT studies on exercise intensity normalisation have investigated this framework (Bartram et al., 2018, Ferguson et al., 2013, Galbraith et al., 2015). However, in a previous study with runners (Galbraith et al., 2015), and a further investigation with elite cyclists (Bartram et al., 2018), HIIT performance predictions based upon the CP model proved inaccurate, posing a challenge to practitioners and researchers.

While it may be difficult to normalise exercise intensity for HIIT across individuals, longitudinal HIIT interventions have been analysed as to the levels of adaptive variability produced (Astorino and Schubert, 2014, Coakley and Passfield, 2018b, Montero and Lundby, 2017, Williams et al., 2019). It could be argued that this outcome results, at least in part, from how training work rates are set for each participant (i.e. a methodological problem) (Iannetta et al., 2020, Jamnick et al., 2020, Mann et al., 2013, Mann et al., 2014). To shed light on this hypothesis, the purpose of this study was to compare methods of intensity prescription for their ability to normalise performance (i.e. TTE), physiological, and perceptual responses to HIIT between individuals. Four existing methods were chosen according with their standing in the scientific literature, which are based upon the following benchmarks: the delta between GET and $\dot{V}O_{2max}$ (Lansley et al., 2011), $\dot{W}_{max}$ (Granata et al., 2018), the mean work rate of a 20-min time-trial (Nimmerichter et al., 2011), and W' (Jones and Vanhatalo, 2017). It was hypothesised that there would be a between-method difference in the magnitude of inter-individual variability in acute HIIT responses.

5.2 – Methods

5.2.1 – Participants

Sixteen male and two female recreationally trained cyclists (age: 38 ± 11 years, height: 177 ± 7 cm, body mass: 71.6 ± 7.9 kg, cycling experience index: 26 ± 5 (see Edwards et al. (2009) for details)) volunteered for this study. Ethical standards compliance is detailed in Chapter 3 – General methods.

5.2.2 – Study design

Participants attended the laboratory on six occasions, at the same time of the day, separated by at least 48 h. In the first visit (Figure 5.1, panels A, B, and C), they completed an incremental test to exhaustion (see Chapter 3 – General methods for details), a 3-min all-out

test, and a 20-min time-trial, sequentially. The last two tests were performed as a familiarisation. In the second visit (Figure 5.1, panels D, E, and F), the 3-min all-out test and the 20-min time-trial were initially repeated in this order. Next, a HIIT session was performed to exhaustion, to familiarise participants with the training format of subsequent visits. Thereafter, participants performed a HIIT session to exhaustion per visit (see Chapter 3 – General methods for details), with different intensity normalisation methods randomly allocated to each of the four visits (see text below for details). Inter-individual variability in performance, physiological and perceptual responses were compared between HIIT sessions.

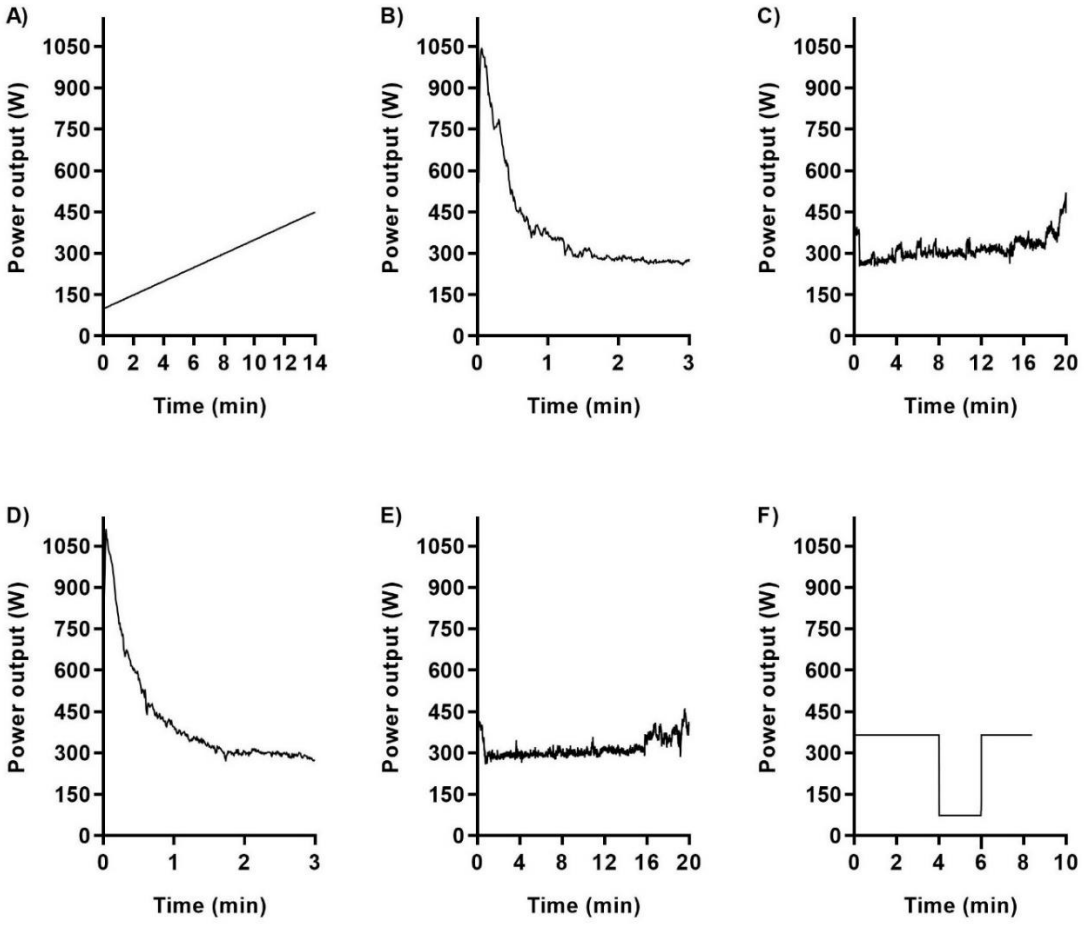

Figure 5.1 – Power output of a representative participant to illustrate the tests performed in the first (panel A: incremental test, panel B: 3-min all-out test, panel C: 20-min time-trial) and second visits (panel D: 3-min all-out test, panel E: 20-min time-trial, panel F: high-intensity interval training session). In the first visit, the 3-min all-out test and the 20-min time-trial were performed as a familiarisation. In the second visit, the high-intensity interval training session was performed as a familiarisation.

All tests started with a 10-min warm-up at 100 W for men, and 50 W for women, except for HIIT sessions (see text below for details). In the first and second visits, tests were separated by 10 min of low-intensity cycling followed by 20 min of rest.

5.2.3 – 3-min all-out test

In the first visit only, following the warm-up, participants were given the chance to practice two 5-s all-out sprints to select the best gear to start the test. A 5-min active recovery was allowed after sprints. Immediately before the test, participants were required to pedal slowly at the optimal gear for 5 s (~150 W). On command, they started an all-out effort for 3 min, with gears being minimally changed (2 or 3 times), always towards the next bigger cog. Despite the strong verbal encouragement provided throughout the test, participants were not informed of elapsed time to prevent pacing. The test was terminated at 185 s to ensure that a full 3-min effort was completed. CP was estimated from the mean power output between 150 and 180 s, and W' from the power output–time integral above CP (Vanhatalo et al., 2007).

5.2.4 – 20-min time-trial

Immediately after the warm-up, participants started the time-trial with the aim of producing the highest possible mean power output for 20 min. They were instructed on how to optimise pacing by observing the graphical feedback on the ergometer screen. Participants drank water and stood on the pedals as desired.

5.2.5 – Intensity prescription

Four intensity normalisation methods were used to set the work rate for the work intervals of each HIIT session: the work rate associated with GET ($\dot{W}_{GET}$) plus 70% of the difference between $\dot{W}_{GET}$ and the work rate associated with $\dot{V}O_{2max}$ (70%Δ – Figure 5.2A); b) 85%$\dot{W}_{max}$ (Figure 5.2B); c) 120% of the mean work rate of the 20-min time-trial (120%TT – Figure 5.2C); d) the work rate predicted to expend 80%W' in 4 min, according with:

$$\dot{W}_{target} = (W' \cdot 0.8)/240 + CP) \quad (5.1)$$

where $\dot{W}_{target}$ is the work rate prescribed (Figure 5.2D). Recovery intervals were always performed at 20% of the work rate prescribed for the work intervals.

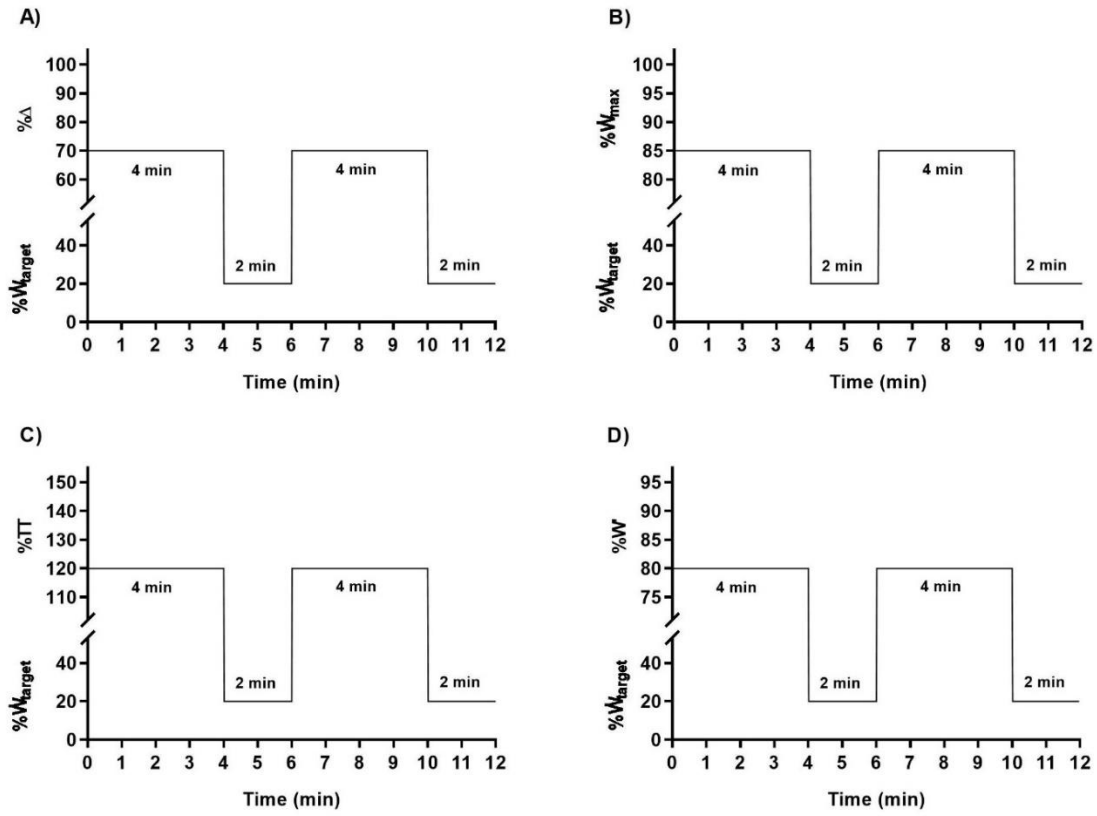

Figure 5.2 – Schematic representation of the high-intensity interval training sessions that participants performed to exhaustion at 70%Δ (panel A), 85%$\dot{W}_{max}$ (panel B), 120%TT (panel C), and 80%W' (panel D), randomly, on four separate occasions. See text for intensity prescription abbreviations. $\dot{W}_{target}$ represents the work rate prescribed for each condition. An identical 10-min warm-up, followed by a two-minute resting period, preceded all sessions. For clarity, these are omitted and only two work intervals are represented.

To ensure that HIIT intensity was comparable on average, the percentage of each prescription benchmark was derived based on pilot work with an independent sample of five male cyclists (age: 28 ± 3 years, height: 173 ± 10 cm, body mass: 66.3 ± 11.2 kg, $\dot{V}O_{2max}$: 59.2 ± 7.1 ml·kg^{-1}·min^{-1}). The work rates for 70%Δ, 85%$\dot{W}_{max}$, 120%TT, and 80%W' corresponded to 4.59 ± 0.76, 4.57 ± 0.66, 4.61 ± 0.65, and 4.67 ± 0.80 W·kg^{-1}, respectively ($F = 0.41$, $P = 0.62$, $\eta_p^2 = 0.09$).

5.2.6 – HIIT sessions

Common procedures and questionnaires are outlined in Chapter 3 – General methods. The same 10-min warm-up was performed before every HIIT session. Two 5-min bouts were performed sequentially at 40% and 50% of the mean work rate prescribed for the work

intervals of all four HIIT sessions. The first work interval started 2 min after the warm-up was terminated. During this resting period, the metabolic cart was set up and participants wore the facemask. In the last 10 s before HIIT sessions started, participants increased cadence to >100 rev·min^{-1}. After participants reached exhaustion, a 3-min rest was allowed, and a cool-down identical to the warm-up was performed.

5.2.7 – Data processing

Raw breath-by-breath gas data were smoothed to 5-s averages. Time >90%$\dot{V}O_{2max}$ and time >95%$\dot{V}O_{2max}$ were calculated for each HIIT session by summing all $\dot{V}O_2$ samples above the established cut-off. Time >90%$\dot{V}O_{2max}$ and time >95%$\dot{V}O_{2max}$ were also calculated as a percentage of TTE (time >90%$\dot{V}O_{2max[\%TTE]}$ and time >95%$\dot{V}O_{2max[\%TTE]}$, respectively). Cadence was analysed as the average of each work interval. $\dot{V}O_2$, HR, $\dot{V}E$, f_R, ΔStO_2, and Δdeoxy[heme] were analysed as the average of the last minute of each work interval, or the completed duration if shorter than one minute (although maximal responses were sometimes elicited during the last complete work interval, but not during the incomplete one).

5.2.8 – Data analysis

Data were assessed for normality using Shapiro-Wilk's test and normal quantile plots. For the dependent variables conforming to a normal distribution, one-way repeated measures analyses of variance were performed to test for systematic differences between conditions (70%Δ, 85%$\dot{W}_{max}$, 120%TT, or 80%W'), with Bonferroni pairwise comparisons used to identify where significant differences existed within the data. As TTE, time >90%$\dot{V}O_{2max}$, and time >95%$\dot{V}O_{2max}$ did not meet the normality assumption, Friedman tests were performed to investigate between-condition differences, with Dunn pairwise comparisons used to identify where significant differences existed within the data. To investigate the magnitude of inter-individual variability in TTE as a function of exercise intensity, all times were first log-transformed (base *e*). Then, the four target work rates calculated for each HIIT session (as 70%Δ, 85%$\dot{W}_{max}$, 120%TT, and 80%W'), for each participant, were also expressed as %$\dot{V}O_{2max}$, %Δ, %$\dot{W}_{max}$, %TT, and %W'. Linear mixed models were fitted to the logarithm of TTE with relative intensity as a fixed factor and participant as a random effect. The inter-individual CV for log-transformed TTE was calculated as:

$$CV\ (\%) = \sqrt{(e^{Var\text{-}1})} \qquad (5.2)$$

where Var is the variance of the log-transformed data. The relationship between both RPE and [La^-] at the end of the first work interval and log-transformed TTE were assessed with correlational analysis adjusted for repeated observations within participants. Linear mixed models were also used to investigate the magnitude of inter-individual variability in $\dot{V}O_2$, RPE, [La^-], HR, $\dot{V}E$, f_R, ΔStO_2, Δdeoxy[heme], and cadence, with participant as a random effect. When appropriate, work interval was considered as a fixed factor, with linear, quadratic, or cubic terms. No specific function was assumed, and optimal model fit was determined statistically based on likelihood ratio tests. Ninety-five percent confidence limits were calculated by bootstrap sampling with 200 repetitions. Systematic differences between conditions were assessed using Prism 8 (GraphPad, San Diego, USA) and data modelling was performed using R 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria). Significance level was set at $P \leq 0.05$. Results are presented as mean ± SD unless otherwise stated. To aid understanding of results, the reader unfamiliarised with linear mixed models is referred to Brown (2021) for a tutorial.

5.3 – Results

During the incremental test, participants attained a $\dot{V}O_{2max}$ of 54.3 ± 8.9 ml·kg^{-1}·min^{-1}, $\dot{W}_{max}$ of 5.01 ± 0.80 W·kg^{-1}, $\dot{W}_{GET}$ of 2.76 ± 0.46 W·kg^{-1}, peak HR of 179 ± 14 beats·min^{-1}, peak respiratory exchange ratio of 1.19 ± 0.05, [La^-] of 12.0 ± 3.3 mmol·L^{-1}, and RPE of 19.5 ± 0.5. Estimated CP and W' following the 3-min all-out test were 3.72 ± 0.73 W·kg^{-1} and 215.7 ± 70.4 J·kg^{-1}, respectively. The mean power output of the 20-min time-trial was 3.65 ± 0.60 W·kg^{-1}. The work and recovery intervals of the HIIT sessions were performed respectively at 4.16 ± 0.65 and 0.83 ± 0.13 W·kg^{-1} for 70%Δ, 4.26 ± 0.68 and 0.85 ± 0.14 W·kg^{-1} for 85%$\dot{W}_{max}$, 4.38 ± 0.72 and 0.88 ± 0.14 W·kg^{-1} for 120%TT, and 4.44 ± 0.82 and 0.89 ± 0.16 W·kg^{-1} for 80%W'. The warm-up/cool-down bouts were performed at 1.72 ± 0.28 and 2.15 ± 0.34 W·kg^{-1}.

No systematic differences between conditions were evident for time >95%$\dot{V}O_{2max}$ ($F_r = 3.73$, $P = 0.29$), time >90%$\dot{V}O_{2max[\%TTE]}$ ($F = 0.61$, $P = 0.56$, $\eta_p^2 = 0.03$), time >95%$\dot{V}O_{2max[\%TTE]}$ ($F = 0.32$, $P = 0.73$, $\eta_p^2 = 0.02$), sRPE ($F = 2.48$, $P = 0.09$, $\eta_p^2 = 0.13$), intrinsic motivation ($F = 0.05$, $P = 0.96$, $\eta_p^2 = 0.00$), success motivation ($F = 1.60$, $P = 0.21$, $\eta_p^2 = 0.09$), sport emotions (all $F \leq 1.81$, $P \geq 0.17$, $\eta_p^2 \leq 0.10$), pre-HIIT sleep duration ($F = 1.36$, $P = 0.27$, $\eta_p^2 = 0.07$), post-HIIT sleep duration ($F = 0.27$, $P = 0.72$, $\eta_p^2 = 0.02$), training diary scales (all $F \leq 1.54$, $P \geq 0.23$, $\eta_p^2 \leq 0.08$), or the NASA-TLX subscales of mental demand ($F = 1.44$, $P =$

0.25, η_p^2 = 0.08), physical demand (F = 0.80, P = 0.49, η_p^2 = 0.04), temporal demand (F = 0.34, P = 0.70, η_p^2 = 0.02), and effort (F = 0.63, P = 0.55, η_p^2 = 0.04).

However, there was a condition effect for the power output ($W \cdot kg^{-1}$; for absolute power output, see Figure 5.3A) at which work (F = 9.56, P < 0.001, η_p^2 = 0.36) and recovery intervals (F = 9.09, P < 0.001, η_p^2 = 0.35) were performed, TTE (F_r = 16.20, P = 0.001 – Figure 5.3B), time >90%$\dot{V}O_{2max}$ (F_r = 10.00, P = 0.018), and the NASA-TLX subscales of performance (F = 3.86, P = 0.027, η_p^2 = 0.19) and frustration (F = 6.46, P = 0.003, η_p^2 = 0.28). Pairwise comparisons revealed that the power outputs ($W \cdot kg^{-1}$) at which work and recovery intervals were performed were lower for 70%Δ compared with all other conditions (all P ≤ 0.033). As a consequence, TTE was longer for 70%Δ compared with 120%TT and 80%W' (both P ≤ 0.022), while time >90%$\dot{V}O_{2max}$ was longer for 70%Δ compared with 120%TT only (P = 0.014). Performance was rated poorer for 120%TT compared with 70%Δ and 85%$\dot{W}_{max}$ (both P ≤ 0.027), and frustration was rated higher for 80%W' compared with 70%Δ and 85%$\dot{W}_{max}$ (both P ≤ 0.035).

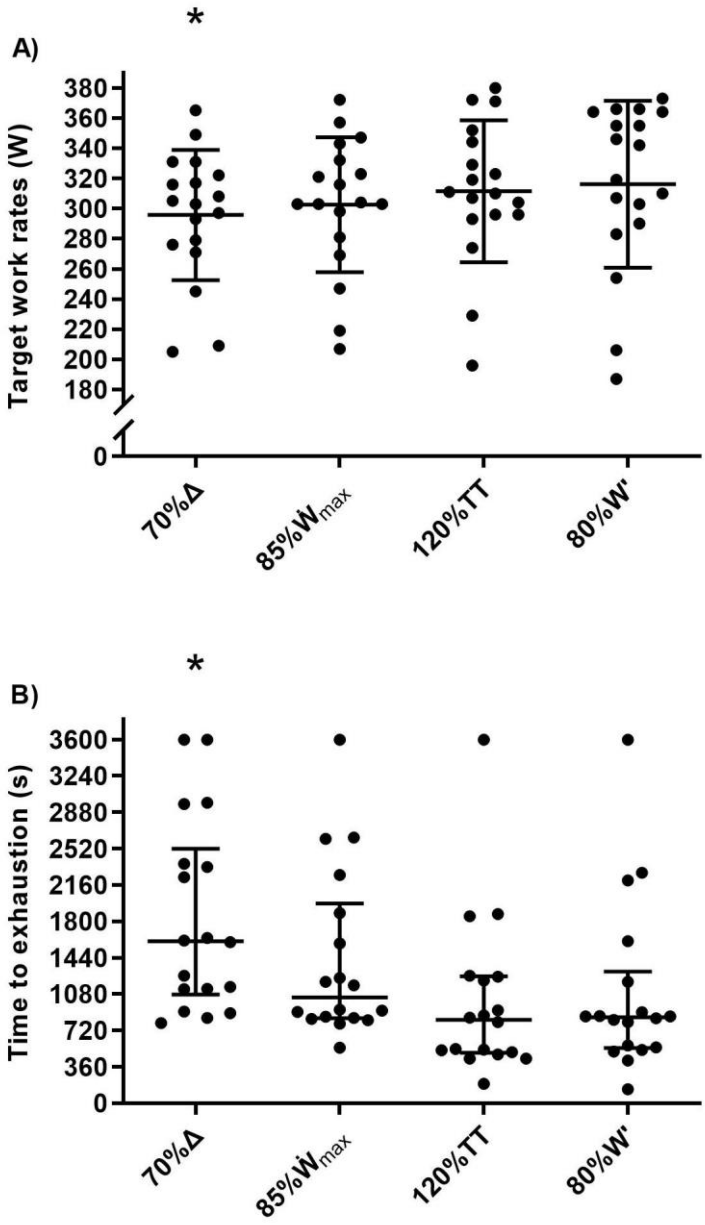

Figure 5.3 – Target work rates for the work intervals of each high-intensity interval training session (panel A), and associated time to exhaustion (panel B). Horizontal bars represent the mean (panel A) and median (panel B), whiskers represent the standard deviation (panel A) and interquartile range (panel B), and dots represent individual measures. Participants were stopped at 3600 s (i.e. end of the 10th work interval; see text for details). * denotes difference from all other conditions in panel A (all $P \leq 0.038$), and difference from 120%TT and 80%W' in panel B (both $P \leq 0.022$). See text for intensity prescription abbreviations.

The median TTEs (25th percentile – 75th percentile) were 26.7 min (17.9 – 42.0 min), 17.4 min (14.0 – 33.0 min), 13.8 min (8.3 – 20.9 min), and 14.2 min (9.1 – 21.7 min), for 70%Δ, 85%$\dot{W}_{max}$, 120%TT, and 80%W', respectively. Estimates of inter-individual variability in

log-transformed TTE as a function of exercise intensity are presented in Table 5.1. There were inverse correlations between both RPE ($r = -0.35$, $R^2 = 0.12$, $P = 0.010$) and $[La^-]$ ($r = -0.52$, $R^2 = 0.27$, $P \leq 0.001$) at the end of the first work interval and log-transformed TTE. Estimates of inter-individual variability in physiological responses, RPE, and cadence for each HIIT condition are presented in Table 5.2. For all variables, confidence intervals overlapped substantially, indicating that all intensity normalisation methods elicited similar magnitudes of inter-individual variability. The magnitude of inter-individual variability in time >90%$\dot{V}O_{2max[\%TTE]}$ and time >95%$\dot{V}O_{2max[\%TTE]}$ was also similar between conditions (Table 5.3).

Table 5.1 – Linear mixed model estimates for the natural logarithm of time to exhaustion (s) [95% confidence limits].

dependent variable	intensity prescription	intercept	intensity coefficient	inter-individual SD	inter-individual CV (%)	standard error of estimate	inter-individual variability (%)	residual variability (%)
$\log_e$ (time to exhaustion (s))	$\%\dot{V}O_{2max}$	20.1 [18.0 – 22.6]	-0.142 [-0.171 – -0.120]	0.476 [0.290 – 0.649]	50.4 [29.6 – 72.4]	0.321 [0.258 – 0.369]	68.7 [44.7 – 82.5]	31.3 [17.0 – 54.8]
	$\%\Delta$	10.4 [9.8 – 11.0]	-0.044 [-0.052 – -0.037]	0.503 [0.326 – 0.703]	53.7 [33.5 – 80.0]	0.335 [0.276 – 0.401]	69.2 [46.2 – 82.3]	30.8 [17.5 – 51.9]
	$\%\dot{W}_{max}$	17.0 [15.1 – 18.9]	-0.116 [-0.138 – -0.096]	0.422 [0.271 – 0.576]	44.2 [27.6 – 62.7]	0.326 [0.259 – 0.389]	62.6 [37.1 – 77.1]	37.4 [22.8 – 59.4]
	%TT	16.6 [14.9 – 18.3]	-0.082 [-0.095 – -0.067]	0.547 [0.318 – 0.740]	59.1 [32.6 – 85.4]	0.326 [0.267 – 0.385]	73.8 [46.1 – 85.1]	26.2 [14.8 – 51.8]
	%W'	8.1 [7.8 – 8.5]	-0.017 [-0.021 – -0.013]	0.466 [0.265 – 0.688]	49.2 [27.0 – 77.8]	0.390 [0.309 – 0.461]	58.9 [31.4 – 75.7]	41.1 [22.9 – 65.7]

Formula: time to exhaustion (s) = $2.718282^{(\text{intercept} + \text{intensity coefficient} \cdot x\%)}$. See text for intensity prescription abbreviations.

Table 5.2 – Linear mixed model estimates for selected responses to exhaustive interval training [95% confidence limits].

dependent variable	intensity prescription	intercept	interval coefficient$_{(a)}$	interval coefficient$_{(b)}$	interval coefficient$_{(c)}$	inter-individual SD	standard error of estimate	inter-individual variability (%)	residual variability (%)
oxygen uptake ($ml \cdot kg^{-1} \cdot min^{-1}$)	70%Δ	50.3 [47.4 – 53.2]	N/A	N/A	N/A	6.6 [4.1 – 9.3]	2.2 [1.9 – 2.6]	89.7 [76.2 – 94.8]	10.3 [5.2 – 23.4]
	85%$\dot{W}_{max}$	50.5 [47.4 – 54.5]	N/A	N/A	N/A	7.4 [4.7 – 9.9]	2.4 [2.0 – 2.8]	90.7 [75.9 – 94.9]	9.3 [5.0 – 23.0]
	120%TT	50.1 [45.9 – 54.2]	N/A	N/A	N/A	8.3 [5.4 – 10.9]	2.5 [2.0 – 3.1]	91.4 [80.6 – 95.4]	8.6 [4.5 – 18.8]
	80%W'	51.2 [47.5 – 55.2]	N/A	N/A	N/A	8.2 [5.3 – 10.3]	2.4 [1.9 – 2.9]	92.3 [83.2 – 95.7]	7.7 [4.1 – 16.5]
ratings of perceived exertion	70%Δ	13.8 [12.9 – 14.7]	1.6 [1.3 – 1.9]	-0.08 [-0.12 – -0.06]	N/A	1.6 [1.0 – 2.2]	1.0 [0.8 – 1.2]	73.5 [49.4 – 84.9]	26.5 [14.8 – 48.2]
	85%$\dot{W}_{max}$	13.1 [11.5 – 14.6]	3.5 [2.2 – 4.9]	-0.55 [-0.94 – -0.25]	0.03 [0.01 – 0.06]	1.4 [0.8 – 2.1]	1.2 [0.9 – 1.5]	57.3 [26.3 – 78.9]	42.7 [21.0 – 72.0]
	120%TT	14.0 [12.7 – 15.2]	2.1 [1.6 – 2.5]	-0.12 [-0.16 – -0.07]	N/A	2.3 [1.4 – 3.3]	1.0 [0.8 – 1.2]	83.8 [65.1 – 92.9]	16.2 [7.0 – 32.2]
	80%W'	13.1 [11.2 – 14.6]	3.5 [2.3 – 4.8]	-0.55 [-0.90 – -0.26]	0.03 [0.01 – 0.05]	1.4 [0.8 – 2.1]	1.2 [0.9 – 1.5]	57.3 [29.2 – 78.6]	42.7 [21.0 – 69.8]

blood lactate concentration ($mmol \cdot L^{-1}$)	70%Δ	4.4 [2.2 – 6.4]	5.0 [3.6 – 6.3]	-0.9 [-1.2 – -0.6]	0.04 [0.03 – 0.06]	2.9 [1.9 – 3.9]	1.6 [1.3 – 1.8]	77.8 [57.2 – 87.6]	22.2 [12.2 – 42.8]
	85%$\dot{W}_{max}$	5.5 [3.6 – 7.1]	4.9 [3.8 – 6.1]	-0.9 [-1.1 – -0.6]	0.05 [0.03 – 0.06]	3.1 [2.0 – 4.1]	1.1 [1.0 – 1.3]	87.8 [74.2 – 93.6]	12.2 [5.9 – 25.4]
	120%TT	5.5 [3.1 – 7.8]	5.9 [4.0 – 8.0]	-1.1 [-1.7 – -0.7]	0.06 [0.03 – 0.10]	3.3 [2.1 – 4.4]	1.6 [1.3 – 1.9]	79.7 [60.5 – 90.3]	20.3 [9.5 – 38.4]
	80%W'	9.3 [7.2 – 11.1]	2.8 [2.0 – 3.4]	-0.3 [-0.4 – -0.2]	N/A	3.2 [1.9 – 4.2]	1.7 [1.3 – 2.0]	78.5 [51.0 – 89.5]	21.5 [10.5 – 47.6]
heart rate ($beats \cdot min^{-1}$)	70%Δ	161 [154 – 168]	5 [3 – 7]	-0.4 [-0.6 – -0.2]	N/A	12 [7 – 16]	6 [5 – 7]	77.0 [55.9 – 87.2]	23.0 [12.6 – 43.2]
	85%$\dot{W}_{max}$	157 [147 – 165]	10 [4 – 14]	-1.9 [-3.1 – -0.6]	0.1 [0.0 – 0.2]	12 [8 – 17]	6 [5 – 7]	80.2 [61.4 – 90.0]	19.8 [9.7 – 37.5]
	120%TT	161 [153 – 167]	5 [2 – 6]	-0.3 [-0.5 – -0.1]	N/A	15 [9 – 21]	4 [3 – 5]	93.7 [85.6 – 97.1]	6.3 [2.8 – 14.3]
	80%W'	164 [158 – 170]	4 [2 – 5]	-0.3 [-0.5 – 0.0]	N/A	11 [8 – 15]	5 [3 – 5]	85.3 [72.0 – 93.2]	14.7 [6.4 – 26.7]
ventilation ($L \cdot min^{-1}$)	70%Δ	125 [115 – 136]	9 [4 – 12]	-0.6 [-0.9 – -0.1]	N/A	19 [13 – 26]	12 [9 – 13]	72.8 [50.8 – 83.5]	27.2 [16.1 – 47.3]
	85%$\dot{W}_{max}$	133 [120 – 146]	7 [2 – 12]	-0.5 [-0.9 – 0.0]	N/A	20 [12 – 27]	11 [9 – 13]	74.7 [49.2 – 87.2]	25.3 [12.8 – 48.8]
	120%TT	131 [118 – 143]	9 [3 – 15]	-0.7 [-1.4 – -0.2]	N/A	20 [14 – 29]	13 [10 – 15]	71.3 [49.0 – 86.8]	28.7 [12.9 – 49.5]
	80%W'	138 [128 – 151]	7 [3 – 10]	-0.5 [-0.8 – 0.0]	N/A	22 [14 – 29]	9 [7 – 11]	84.2 [67.2 – 92.8]	15.8 [7.1 – 31.7]

respiratory frequency (cycles·min^{-1})	70%Δ	43 [38 – 48]	5 [3 – 6]	-0.2 [-0.3 – -0.1]	N/A	12 [8 – 15]	4 [4 – 5]	87.9 [74.9 – 92.6]	12.1 [7.4 – 24.3]
	85%$\dot{W}_{max}$	45 [39 – 51]	5 [4 – 7]	-0.4 [-0.5 – -0.2]	N/A	10 [7 – 13]	4 [3 – 4]	88.4 [72.6 – 93.3]	11.6 [6.5 – 25.5]
	120%TT	39 [33 – 46]	13 [8 – 17]	-2.2 [-3.4 – -1.1]	0.1 [0.0 – 0.2]	11 [7 – 14]	4 [3 – 4]	89.3 [78.0 – 95.0]	10.7 [5.0 – 21.0]
	80%W'	43 [36 – 49]	9 [5 – 14]	-1.4 [-2.6 – -0.5]	0.1 [0.0 – 0.1]	11 [7 – 15]	4 [3 – 4]	90.8 [80.2 – 96.1]	9.2 [3.8 – 18.7]
ΔStO_2 (%)	70%Δ	-21.4 [-24.5 – -18.3]	-0.4 [-0.6 – -0.1]	N/A	N/A	7.0 [4.3 – 9.5]	2.8 [2.3 – 3.2]	86.5 [68.9 – 93.2]	13.5 [6.7 – 30.1]
	85%$\dot{W}_{max}$	-20.9 [-23.3 – -17.9]	-0.3 [-0.5 – -0.1]	N/A	N/A	5.1 [3.2 – 6.7]	1.4 [1.1 – 1.6]	93.2 [84.1 – 96.5]	6.8 [3.4 – 15.8]
	120%TT	-21.7 [-25.5 – -17.4]	1.5 [-0.3 – 3.1]	-0.4 [-0.7 – -0.1]	N/A	6.8 [4.1 – 9.9]	1.7 [1.3 – 2.1]	94.3 [85.1 – 97.6]	5.7 [2.2 – 14.9]
	80%W'	-19.4 [-22.3 – -16.6]	-0.5 [-0.7 – -0.3]	N/A	N/A	5.7 [3.7 – 7.6]	1.3 [1.0 – 1.6]	95.3 [88.1 – 97.9]	4.7 [2.1 – 11.5]
Δdeoxy[heme] (μm)	70%Δ	84 [69 – 100]	1.5 [0.6 – 2.3]	N/A	N/A	32 [20 – 42]	10 [8 – 11]	91.4 [80.6 – 95.2]	8.6 [4.7 – 18.6]
	85%$\dot{W}_{max}$	80 [69 – 95]	1.1 [0.2 – 1.8]	N/A	N/A	21 [13 – 28]	6 [5 – 7]	92.7 [80.1 – 96.3]	7.3 [3.5 – 18.8]
	120%TT	79 [64 – 91]	1.7 [0.3 – 3.0]	N/A	N/A	29 [19 – 39]	5 [4 – 6]	97.3 [93.0 – 98.9]	2.7 [1.1 – 7.0]
	80%W'	82 [67 – 96]	1.9 [0.7 – 3.0]	N/A	N/A	32 [21 – 44]	6 [5 – 7]	96.3 [91.4 – 98.2]	3.7 [1.6 – 8.0]

cadence ($rev \cdot min^{-1}$)	70%Δ	102 [98 – 107]	-2 [-2 – -1]	N/A	N/A	9 [6 – 12]	5 [4 – 6]	74.7 [53.6 – 85.3]	25.3 [14.7 – 45.6]
	85%$\dot{W}_{max}$	101 [97 – 105]	-2 [-2 – -1]	N/A	N/A	8 [5 – 11]	6 [4 – 6]	74.3 [48.6 – 87.3]	25.7 [12.3 – 51.0]
	120%TT	100 [94 – 104]	-2 [-3 – -1]	N/A	N/A	9 [5 – 13]	6 [5 – 7]	68.9 [43.0 – 83.3]	31.1 [16.6 – 56.3]
	80%W'	100 [95 – 105]	-2 [-3 – -1]	N/A	N/A	9 [6 – 12]	5 [4 – 6]	77.0 [55.9 – 89.0]	23.0 [10.9 – 43.8]

Formula: dependent variable = intercept + interval coefficient$_{(a)} \cdot x$ + interval coefficient$_{(b)} \cdot x^2$ + interval coefficient$_{(c)} \cdot x^3$, where x = work interval number. ΔStO_2, changes from a resting baseline in muscle tissue oxygen saturation; Δdeoxy[heme], changes from a resting baseline in the concentration of deoxygenated heme compounds; N/A, not applicable (i.e. consider the coefficient as 0). See text for intensity prescription abbreviations.

Table 5.3 – Central tendency and dispersion measures for time >90%$\dot{V}O_{2max}$ and time >95%$\dot{V}O_{2max}$ [95% confidence limits].

intensity prescription	time >90%$\dot{V}O_{2max}$ (s)		time >95%$\dot{V}O_{2max}$ (s)		time >90%$\dot{V}O_{2max[\%TTE]}$		time >95%$\dot{V}O_{2max[\%TTE]}$	
	Median	Q1 - Q3	Median	Q1 - Q3	Mean	SD	Mean	SD
70%Δ	478*	346 - 633	143	65 - 345	32.8 [25.1 – 40.5]	15.5 [11.7 – 23.3]	17.4 [9.7 – 25.0]	15.4 [11.5 – 23.1]
85%$\dot{W}_{max}$	385	300 - 720	168	83 - 439	36.5 [29.6 – 43.3]	13.8 [10.3 – 20.7]	19.0 [11.9 – 26.0]	14.2 [10.7 – 21.3]
120%TT	275	113 - 430	148	15 - 225	32.2 [22.7 – 41.8]	19.3 [14.5 – 28.9]	16.5 [9.5 – 23.5]	14.1 [10.6 – 21.1]
80%W'	338	141 - 434	98	44 - 255	36.1 [28.1 – 44.1]	16.0 [12.0 – 24.0]	19.7 [11.7 – 27.7]	16.0 [12.0 – 24.0]

Q1, 25th percentile; Q3, 75th percentile. * denotes difference from 120%TT (P = 0.014). See text for intensity prescription abbreviations.

5.4 – Discussion

This study focused on the methodological aspect of intensity prescription for HIIT. By assessing inter-individual variability in performance, physiological and perceptual responses to HIIT sessions randomly prescribed to cyclists at 70%Δ, 85%$\dot{W}_{max}$, 120%TT, and 80%W', it was sought to identify the optimal approach to normalise exercise intensity. In other words, it was expected that at least one prescription method would minimise the magnitude of inter-individual variability in acute HIIT responses. However, it was not possible to detect clear evidence, be it performance-related, physiological, or perceptual, to support the use of one method over the others. For instance, log-transformed TTE was modelled as a function of exercise intensity and similar magnitudes of inter-individual variability were observed for all normalisation methods. Given the pooled median TTE of 15.3 min, and wide interquartile ranges of 24.1, 19.0, 12.6, and 12.6 min for respectively 70%Δ, 85%$\dot{W}_{max}$, 120%TT, and 80%W', these intensity normalisation methods may be considered inappropriate for prescription of HIIT.

5.4.1 – Methodological aspects

Previous studies investigating exercise intensity normalisation (Baldwin et al., 2000, Bartram et al., 2018, Coyle et al., 1988, Egger et al., 2016, Ferguson et al., 2013, Galbraith et al., 2015, Iannetta et al., 2020, Julio et al., 2020, Lansley et al., 2011, McLellan and Skinner, 1985, Meyer et al., 1999, Scharhag-Rosenberger et al., 2010) can be categorised according with their experimental design, from the least to most robust approach for the evaluation of a method: a) individualised work rate targets based on percentages of a maximal benchmark (e.g. 70%$\dot{V}O_{2max}$, 60%$\dot{W}_{max}$) are expressed relative to a criterion intensity-domain transition marker (e.g. %$\dot{W}_{GET}$, %CP), with resultant variability quantified (Iannetta et al., 2020, Meyer et al., 1999); b) bouts of exercise are performed at work rates normalised to one or more benchmarks, with raw variability in individual exercise responses, or agreement between predicted and actual responses, quantified (Baldwin et al., 2000, Bartram et al., 2018, Coyle et al., 1988, Ferguson et al., 2013, Galbraith et al., 2015, Julio et al., 2020, Lansley et al., 2011, Scharhag-Rosenberger et al., 2010); c) exercise responses at multiple timepoints or conditions are modelled as a function of different benchmarks to minimise the influence of random variability over estimates of inter-individual variability (present study, McLellan and Skinner (1985), and Egger et al. (2016)). While methodological differences preclude direct comparison of present results with those of other studies, it was possible to draw general conclusions by reanalysing raw data directly

available in tables or through data extraction from figures with WebPlotDigitizer (http://automeris.io/WebPlotDigitizer). Inter-individual variability was quantified as SD or CV. If TTE with mean *t* is considered, it is expected that approximately 68.2% of the individuals sampled from a population will reach exhaustion in between *t* – SD and *t* + SD, or between *t* – $CV_{(\%t)}$ and *t* + $CV_{(\%t)}$. For example, if *t* = 1000 s, and SD = 400 s, CV will be 40%. Hence, approximately 68.2% of the individuals sampled from a population will reach exhaustion in between 600 and 1400 s. Being CV relative to the mean, it is sometimes possible to extrapolate a given estimate to other samples with different means.

5.4.2 – Performance variability

Several authors have recommended that $\%\dot{V}O_{2max}$, the traditional approach to normalising exercise intensity, is abandoned (Baldwin et al., 2000, Coyle et al., 1988, Egger et al., 2016, Iannetta et al., 2020, Jamnick et al., 2020, Lansley et al., 2011, Mann et al., 2013, McLellan and Skinner, 1985, Meyer et al., 1999, Rossiter, 2011, Scharhag-Rosenberger et al., 2010). In this study, with HIIT performed at approximately 92.3%$\dot{V}O_{2max}$, the inter-individual CV for log-transformed TTE was 50.4%. This figure suggests that HIIT normalised to $\%\dot{V}O_{2max}$ may elicit similar or slightly greater performance variability than constant-intensity exercise, given the inter-individual CVs of 42.8%, 43.4%, 42.5%, and 41.8% estimated for constant-intensity exercise at approximately 75% (Scharhag-Rosenberger et al., 2010), 88.2% (Coyle et al., 1988), 90% (Lansley et al., 2011), and 94.8%$\dot{V}O_{2max}$ (McLellan and Skinner, 1985), respectively. While the present study reinforces the consensual view about $\%\dot{V}O_{2max}$, none of the alternative methods evaluated performed better (see Table 5.1). In contrast to what has been shown for constant-intensity exercise, in which %Δ may decrease performance variability (Lansley et al., 2011, McLellan and Skinner, 1985), inter-individual CVs for log-transformed TTE varied from 44.2% ($\%\dot{W}_{max}$) to 69.1% (%TT), with confidence intervals of all prescriptions overlapping substantially, and lower limits of approximately 30%.

A popular approach to normalising exercise intensity for HIIT consists of using individuals' CP and W' (Bartram et al., 2018, Ferguson et al., 2013, Galbraith et al., 2015, Jones and Vanhatalo, 2017). Ferguson et al. (2013) asked eight active men to perform three HIIT sessions (running) to exhaustion, all with four-minute work and recovery intervals ($HIIT_{4min/4min}$), at work rates predicted to expend 100%W' in 4, 6, and 8 min. The inter-individual CVs for TTE were 20.3%, 20.3%, and 22.8%, respectively. Even with a similar HIIT format and total exercise duration, the present study does not corroborate Ferguson's

findings (Ferguson et al., 2013), given the CV of 49.2% for log-transformed TTE as a function of %W'. A likely reason resides in the fact that a 3-min all-out test was used in the present study to avoid excessive participant burden, whereas Ferguson et al. (2013) adopted four constant-work rate bouts to determine CP and W'. While the 3-min all-out test was initially considered valid (Vanhatalo et al., 2007), more recent studies have questioned its use with trained cyclists (Bartram et al., 2017, Nicolò et al., 2017a). Interestingly, Julio et al. (2020) have shown that the inter-individual CV for running TTE can be reduced from 45.2% to 21.8% when HIIT with fifteen-second work and recovery intervals ($HIIT_{15s/15s}$) is prescribed relative to the anaerobic speed reserve rather than $\dot{W}_{max}$. Taken together, the results of Ferguson (Ferguson et al., 2013) and Julio (Julio et al., 2020) suggest that an inter-individual CV of approximately 20% for TTE is an achievable target, although several popular methods of exercise intensity normalisation may fail to produce such an outcome.

5.4.3 – Physiological variability

From a physiological standpoint, [La^-] responses to HIIT varied substantially between individuals, with no between-condition differences in magnitude to suggest there was an optimal method for exercise intensity normalisation. Here, a CV would be less intelligible due to the rising pattern observed after each work interval (see interval coefficients in Table 5.2). Nevertheless, previous studies have frequently used [La^-] as a marker of metabolic stress (Baldwin et al., 2000, Coyle et al., 1988, Egger et al., 2016, Ferguson et al., 2013, Julio et al., 2020, Lansley et al., 2011, Meyer et al., 1999, Scharhag-Rosenberger et al., 2010) and provide a reference to put numbers in perspective. The inter-individual SD for [La^-] during HIIT varied from 2.9 (70%Δ) to 3.3 mmol·L^{-1} (120%TT), with lower confidence limits of approximately 2.0 mmol·L^{-1} for all prescriptions. Coyle et al. (1988) reported [La^-] of 11.0 ± 4.4 mmol·L^{-1} immediately after exhaustion when cyclists performed constant-intensity exercise at 88.2%$\dot{V}O_{2max}$. Julio et al. (2020) reported [La^-] changes from resting to exhaustion of 7.7 ± 3.4 mmol·L^{-1} when $HIIT_{15s/15s}$ was prescribed as 110%$\dot{W}_{max}$. While these figures indicate the levels of inter-individual variability found in the present study are not unusual for high-intensity exercise, the data obtained by Ferguson et al. (2013) are remarkably more homogenous. Their three $HIIT_{4min/4min}$ sessions, at work rates predicted to expend 100%W' in 4, 6, and 8 min, led to [La^-] at exhaustion of 9.7 ± 1.1, 8.5 ± 1.5, and 8.0 ± 1.1 mmol·L^{-1}, respectively. Indeed, these SDs are just slightly higher than those modelled by Egger et al. (2016) across different submaximal intensities and taking into account intra-individual variability (i.e. 0.6, 0.9, 0.4, and 0.5 mmol·L^{-1} for exercise intensity expressed as

$\%\dot{V}O_{2max}$, $\%\dot{V}O_{2reserve}$, $\%HR_{max}$, and $\%HR_{reserve}$, respectively); and comparable to those reported by studies in which constant-intensity exercise was performed at a much lower intensity (i.e. $75\%\dot{V}O_{2max}$), with $[La^{-}]$ of 4.6 ± 1.9 (Scharhag-Rosenberger et al., 2010) and 2.8 ± 1.1 $mmol \cdot L^{-1}$ (Meyer et al., 1999). It may be speculated that using CP and W' determined from four bouts of constant-work rate exercise, as employed by Ferguson et al. (2013), minimises inter-individual variability in $[La^{-}]$ in addition to TTE. However, this possibility should be scrutinised in light of Ferguson's (Ferguson et al., 2013) sample of only eight individuals.

Given that $[La^{-}]$ plays a central role in the co-ordination of metabolic responses to exercise (Ferguson et al., 2018), it is unsurprising that most studies on exercise intensity normalisation have drawn conclusions from inter-individual variability in $[La^{-}]$ as a marker of exercise intensity (Baldwin et al., 2000, Egger et al., 2016, Julio et al., 2020, Lansley et al., 2011, Meyer et al., 1999, Scharhag-Rosenberger et al., 2010). However, only 27% of TTE variability was accounted for by $[La^{-}]$ measured at 4 min (i.e. at the end of the first work interval), whereas for constant-intensity bouts, 59% (McLellan and Skinner, 1985) and 75% (Sassi et al., 2006) of TTE variability was accounted for by $[La^{-}]$ measured at 6 and 10 min, respectively. The estimate of the present study therefore reinforces the need for a multivariate approach to investigate exercise intensity normalisation (Egger et al., 2016), particularly in the context of HIIT.

Cardiorespiratory responses tend not to achieve steady state during HIIT, increasing continuously towards maximal values within and between work intervals (Rossiter, 2011). For this reason, a snapshot of responses elicited by each four-minute work interval was obtained by averaging measures recorded from the third to the fourth minute, although some information is lost with this approach. HR, $\dot{V}E$, and f_R increased after each work interval (see interval coefficients in Table 5.2), approaching maximal values near exhaustion, consistent with exercise responses to constant-intensity bouts performed in the very heavy domain (Horstman et al., 1979, Lansley et al., 2011, Marcora and Staiano, 2010, Rossiter, 2011). However, all model parameters were very similar between HIIT sessions, providing no evidence for an optimal intensity normalisation method.

Interestingly, work interval number did not affect $\dot{V}O_2$, suggesting that most participants reached a high $\%\dot{V}O_{2max}$ from the first work interval onwards. Indeed, intercepts for $\dot{V}O_2$

varied from 50.1 (120%TT) to 51.2 ml·kg^{-1}·min^{-1} (80%W'), representing 92.3% and 94.3%$\dot{V}O_{2max}$, respectively. Inter-individual variability was also similar across HIIT sessions, with SDs varying from 6.6 (70%Δ) to 8.3 ml·kg^{-1}·min^{-1} (120%TT), and overlapping confidence intervals. From a training perspective, exercise time at or near $\dot{V}O_{2max}$ has been used as a marker of adaptive potential of HIIT sessions, based on the premise that such intensities impose maximum stress on the physiological processes and structures determining $\dot{V}O_{2max}$ (Buchheit and Laursen, 2013). In this regard, 70%Δ elicited longer time >90%$\dot{V}O_{2max}$ compared with 120%TT in the current study (see Table 5.3), likely due to a longer TTE compared with both 120%TT and 80%W' (see Figure 5.3). The difference nevertheless disappeared, and data became remarkably similar across HIIT sessions when time >90%$\dot{V}O_{2max}$ was expressed relative to TTE, both in terms of means and SDs. Altogether, the evidence refutes the hypothesis that $\dot{V}O_2$ responses to HIIT can be better normalised with one prescription method versus another, as demonstrated for constant-intensity exercise (Lansley et al., 2011).

Unique to the present study was the adoption of near-infrared spectroscopy to assess inter-individual variability in tissue oxygenation of the vastus lateralis muscle. Specifically, Δdeoxy[heme] represents the extent to which oxygen is extracted from the perfusing blood, whereas ΔStO_2 represents the relative balance between oxygen delivery and uptake (Barstow, 2019). Accordingly, Δdeoxy[heme] increases and ΔStO_2 decreases as exercise intensity increases, although these relationships are not linear (Boone et al., 2016, Stöcker et al., 2017). In contrast to $\dot{V}O_2$, Δdeoxy[heme] slightly increased and ΔStO_2 slightly decreased after each work interval, suggesting a progressive deterioration of oxygen delivery as per the Fick principle (Fick, 1870), presumably due to cardiac output redistribution towards the respiratory muscles (Harms et al., 1997, Turner et al., 2013). The increments in $\dot{V}E$ and f_R observed after each work interval support this interpretation. Regardless, all tested methods of exercise intensity normalisation elicited similar inter-individual SDs, with overlapping confidence intervals. Therefore, it remains to be determined whether near-infrared spectroscopy, with all of its methodological challenges (Barstow, 2019), would be sensitive to quantifying inter-individual variability in muscle tissue oxygenation.

5.4.4 – Perceptual variability

While it is most common to investigate performance variability from a physiological point of view (Bossi et al., 2017, McLellan and Skinner, 1985, Sassi et al., 2006), RPE has been

shown to predict TTE during constant-intensity bouts performed in the very heavy domain (Horstman et al., 1979, Marcora and Staiano, 2010). For instance, Marcora and Staiano (2010) identified that 67% of TTE variability was accounted for by RPE measured at 8 min. In contrast, RPE at 4 min (i.e. at the end of the first work interval) accounted for only 12% of TTE variability in the present study, suggesting that performance during HIIT may be more unpredictable compared with constant intensity bouts.

Lansley et al. (2011) has previously shown that inter-individual variability in RPE at 5 min can be reduced when constant-intensity exercise is performed at 80%Δ (18 ± 1) as opposed to 90%$\dot{V}O_{2max}$ (19 ± 2). However, these measures were obtained too close to exhaustion (i.e. 8.6 ± 1.8 and 5.4 ± 2.3 min, respectively), constraining inter-individual variability as ratings were bounded to 20. This makes it difficult to compare the present results with those of Lansley (Lansley et al., 2011). It is interesting, however, that across all variables of interest, modelled RPE produced the lowest inter-individual SDs relative to the standard error of estimate (see Table 5.2). While it is conceivable that RPE as a marker of exercise intensity could be more sensitive than other physiological variables, none of the normalisation methods investigated stood out, with SDs varying from 1.4 (85%$\dot{W}_{max}$ and 80%W') to 2.3 (120%TT) and overlapping confidence intervals. Thus, further research is required to validate the use of RPE as a tool to investigate the best methods of exercise intensity normalisation.

5.4.5 – Implications. Because exercise intensity purportedly regulates both acute and chronic (i.e. adaptive) responses to respectively single and repeated bouts of exercise (Granata et al., 2018, MacInnis and Gibala, 2017, Wenger and Bell, 1986), physiologists have tried to identify optimal approaches for its normalisation (Jamnick et al., 2020, Mann et al., 2013). While the present study does not offer a solution in this regard, there are several implications. For instance, the large inter-individual variability in the relationship between intensity and TTE during HIIT, irrespective of how intensity was expressed, poses a challenge to practitioners and researchers. Consider this hypothetical scenario: a coach prescribes to three cyclists a few HIIT sessions for $\dot{V}O_{2max}$ enhancement, with six four-min work intervals at 80%$\dot{W}_{max}$. Cyclist one repeatedly fails to complete the session at the target work rate, cyclist two finds the session too easy, and cyclist three completes the session at the very limit of tolerance. Besides the fact that cyclists one and two might question the coach's ability to appropriately prescribe HIIT, it is possible that only cyclist three will

manifest the desired adaptive effect (i.e. $\dot{V}O_{2max}$ increase), based on the premise that the magnitude of adaptive responses reflects, at least partially, the magnitude of the training stimulus (Flück, 2006, Mann et al., 2014, Perry et al., 2010). Another possible problem may arise when scientists prescribe HIIT to a group of research participants and some are unable to complete the session, potentially leading to their exclusion from the sample, and ultimately biasing estimates of variables under investigation. Finally, our findings are in line with the contention that some of the inter-individual variability in adaptive responses following HIIT programmes (Astorino and Schubert, 2014, Coakley and Passfield, 2018b, Montero and Lundby, 2017, Williams et al., 2019) may result from how intensity was normalised across participants (Iannetta et al., 2020, Jamnick et al., 2020, Mann et al., 2013, Mann et al., 2014).

From an analytical perspective, any gross estimate of inter-individual variability (i.e. not modelled) is subject to overestimation because it does not take into account measurement error and day-to-day biological variability (Egger et al., 2016). To address this requirement, multiple timepoints or conditions should be modelled together, and at least one condition should be repeated (Egger et al., 2016). While in the current study the repetition requirement was achieved for TTE by expressing the four target work rates of each participant as $\%\dot{V}O_{2max}$, %Δ, $\%\dot{W}_{max}$, %TT, and %W', this was not the case for physiological and perceptual responses. This means that modelled SDs for these latter responses did not account for day-to-day variability, potentially overestimating the true inter-individual variability elicited by each method of intensity prescription. However, modelled inter-individual estimates are rare in the literature, with few studies using this approach (Egger et al., 2016, McLellan and Skinner, 1985). Thus, the higher unpredictability of acute HIIT responses in this investigation compared with referenced studies is not merely the result of statistical artefacts.

5.4.6 – Limitations

Despite the best efforts to eliminate potential sources of methodological bias, the results of this study's pilot work were slightly skewed in the sense that 70%Δ ended up being a lower exercise intensity (in watts) compared with $85\%\dot{W}_{max}$, 120%TT, and 80%W'. Unsurprisingly, TTE was longer compared with 120%TT and 80%W'. However, there is no evidence to suggest that results would have been different had HIIT been prescribed at 75%Δ rather than 70%Δ. Besides, performance was rated poorer for 120%TT compared with 70%Δ

and 85%$\dot{W}_{max}$, and frustration was rated higher for 80%W' compared with 70%Δ and 85%$\dot{W}_{max}$, likely as a consequence of the short median TTEs of these conditions. As participants were blinded to the target power outputs, some were clearly disappointed at the end of their "training sessions". Nevertheless, it would have been very difficult to demand that all participants exercised to exhaustion had the relative intensity of all prescriptions been decreased. Indeed, in five HIIT sessions (out of seventy-two), participants completed ten work intervals (the pre-set maximum), although in all these instances they rated an RPE of 20 for the last work interval, suggesting they were very close to exhaustion.

5.4.7 – Conclusions

In summary, the evidence reported in this study suggests that methods of intensity prescription that are often deemed scientifically valid do not normalise acute responses to HIIT between individuals. TTE as a measure of HIIT performance, [La^{-}], RPE, cardiorespiratory responses, and muscle tissue oxygenation were all equally variable between individuals when expressed as %Δ, %$\dot{W}_{max}$, %TT, or %W'. Further studies are required to determine the optimal approach for exercise intensity normalisation of HIIT.

Chapter 6 – Optimizing interval training through power output variation within the work intervals

6.1 – Introduction

HIIT involves repeated bouts of high-intensity exercise interspersed with recovery periods. This method is typically employed to increase the training stimulus for the cardiorespiratory system over prolonged continuous exercise. Accordingly, much of the scientific work related to HIIT has focused on $\dot{V}O_{2max}$ improvements (Bacon et al., 2013, Billat, 2001, Buchheit and Laursen, 2013, Midgley and Mc Naughton, 2006); as the upper limit to the aerobic metabolism and a key determinant of endurance performance (Joyner and Coyle, 2008). It has been suggested that exercising at high intensities is beneficial for improving $\dot{V}O_{2max}$ (Bacon et al., 2013), particularly in the case of well-trained athletes (Billat, 2001, Buchheit and Laursen, 2013, Midgley and Mc Naughton, 2006). Therefore, accumulating time at or close to $\dot{V}O_{2max}$ (e.g. >90% or >95%) during a HIIT session may be important for training adaptation (Bacon et al., 2013, Billat, 2001, Buchheit and Laursen, 2013, Lisbôa et al., 2015, Midgley and Mc Naughton, 2006, Rønnestad and Hansen, 2016, Turnes et al., 2016, Zadow et al., 2015).

Previously, Billat et al. (2013) have demonstrated that the ability to sustain exercise at >95%$\dot{V}O_{2max}$ can exceed 15 min if power output is continuously adjusted according to expired gas responses. In comparison, constant work rate exercise or HIIT performed to exhaustion produces time at >90% or >95%$\dot{V}O_{2max}$ of only a few minutes (Billat, 2001, Billat et al., 2013, Buchheit and Laursen, 2013, Lisbôa et al., 2015, Midgley and Mc Naughton, 2006, Rønnestad and Hansen, 2016). Billat et al. (2013) used a protocol that commenced at the lowest power output eliciting $\dot{V}O_{2max}$ and, once attained, power output was decreased progressively. Subsequently, power output was regulated as per individual $\dot{V}O_2$ responses, enabling >95%$\dot{V}O_{2max}$ to be sustained and TTE prolonged (Billat et al., 2013). While this laboratory protocol is appealing as a training session, it is not practical for the majority of athletes. Alternatively, a HIIT session in which the work intervals include power output variations might provide similar means to increase time at >90%$\dot{V}O_{2max}$.

Previous research suggests that power output distribution affects physiological responses during standardized HIIT sessions (Lisbôa et al., 2015, Zadow et al., 2015), with increased time at >90%$\dot{V}O_{2max}$ following decreasing- versus constant-intensity work intervals (Lisbôa et al., 2015), and greater time at >85%$\dot{V}O_{2max}$ following all-out versus constant-intensity work intervals being reported (Zadow et al., 2015). Although the aforementioned studies did not investigate potential mechanisms, authors attributed the results to a difference in $\dot{V}O_2$

kinetics between HIIT modes (Lisbôa et al., 2015, Zadow et al., 2015), as faster $\dot{V}O_2$ kinetics have been observed during decreasing- versus constant-intensity single bouts of exercise matched for mean power output (Bailey et al., 2011, Jones et al., 2008b). It is believed that $\dot{V}O_2$ kinetics reflect changes in oxidative metabolism within the muscle (Jones et al., 2011, Rossiter et al., 2002), which in turn respond to the energy state of the cells, in particular, the concentration of adenosine diphosphate (ADP) (Wilson, 2017). Higher work rates elevate ADP concentrations and activate oxidative phosphorylation more rapidly (Wilson, 2015), ultimately producing faster $\dot{V}O_2$ kinetics at the onset of decreasing- compared to constant-intensity exercise (Bailey et al., 2011, Jones et al., 2008b). This mechanism leads to the possibility that multiple changes in power output within the first half of a work interval would maximize time at >90%$\dot{V}O_{2max}$.

Despite the attractiveness of the $\dot{V}O_2$ kinetics hypothesis, ventilatory variables such as $\dot{V}E$ or f_R have been largely ignored as part of the physiological responses to different patterns of power output distribution (Bailey et al., 2011, Jones et al., 2008b, Lisbôa et al., 2015, Zadow et al., 2015). As the oxygen cost of hyperpnoea at high-intensity exercise is substantial, reaching 15% of $\dot{V}O_{2max}$ in some individuals (Aaron et al., 1992b, Dominelli et al., 2015), exacerbated ventilatory responses caused by varied-intensity work intervals may help to explain an increased time at >90%$\dot{V}O_{2max}$ in this type of HIIT. Indeed, evidence suggests work rate magnitude affects ventilatory response dynamics (Casaburi et al., 1989). However, the strong association reported between f_R and RPE (Nicolò et al., 2017b) suggests the extra respiratory drive may be associated with a higher perceptual strain and premature fatigue (Harms et al., 2000), potentially offsetting the benefits of being able to spend a longer time at >90%$\dot{V}O_{2max}$.

The purpose of this study was to compare the physiological and perceptual responses elicited by work intervals matched for duration and mean power output, but differing in power output distribution. Specifically, constant-intensity work intervals were prescribed in one HIIT session, whereas power output was repeatedly varied within the work intervals of the other one. The following hypotheses were tested: higher %$\dot{V}O_{2max}$ would be sustained in the varied-intensity mode, and ventilatory variables would predict changes in $\dot{V}O_2$ response.

6.2 – Methods

6.2.1 – Participants

Fourteen well-trained male cyclists (see Table 6.1) volunteered for this study during their off-season. Ethical standards compliance is detailed in Chapter 3 – General methods.

Table 6.1 – Participants' characteristics and preliminary testing results (mean ± SD).

Age (years)	24 ± 6
Height (cm)	184 ± 5
Body mass (kg)	75.0 ± 5.2
$\dot{V}O_{2max}$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	69.2 ± 6.6
$\dot{V}O_{2max}$ ($L \cdot min^{-1}$)	5.16 ± 0.35
$\dot{W}_{max}$ ($W \cdot kg^{-1}$)	5.77 ± 0.66
$\dot{W}_{max}$ (W)	430 ± 35
MAP ($W \cdot kg^{-1}$)	5.18 ± 0.56
MAP (W)	387 ± 33
HR_{max} ($b \cdot min^{-1}$)	191 ± 9
$[La^{-}]_{peak}$ ($mmol \cdot L^{-1}$)	13.3 ± 1.3
$\dot{V}E_{peak}$ ($L \cdot min^{-1}$)	211 ± 17
f_{Rpeak} ($cycles \cdot min^{-1}$)	63 ± 10
V_{Tpeak} (L)	3.4 ± 0.5
RER_{peak}	1.19 ± 0.04
RPE_{peak}	19.4 ± 0.6
4 $mmol \cdot L^{-1}_{LT}$ ($W \cdot kg^{-1}$)	3.77 ± 0.53
4 $mmol \cdot L^{-1}_{LT}$ (W)	282 ± 34
CEI	26 ± 6
Races in the previous season	13 ± 11
Training in the previous season (h)	523 ± 218
Current training ($h \cdot week^{-1}$)	11 ± 5

$\dot{V}O_{2max}$: maximal oxygen uptake; $\dot{W}_{max}$: maximal work rate during the incremental test; MAP: maximal aerobic power; HR_{max}: maximal heart rate; $[La^{-}]_{peak}$: peak blood lactate concentration; $\dot{V}E_{peak}$: peak minute ventilation; f_{Rpeak}: peak respiratory frequency; V_{Tpeak}: peak tidal volume; RER_{peak}: peak respiratory exchange ratio; RPE_{peak}: peak rating of perceived exertion; LT: lactate threshold; CEI: cycling experience index (see text for details).

6.2.2 – Study design

Participants visited the laboratory on three occasions, at the same time of the day, separated by at least 48 h. In the first visit, participants completed a submaximal lactate threshold test and a maximal incremental test to characterize their cycling ability and physiological profile. They were also familiarized with the HIIT sessions used during subsequent visits. In visits two and three, participants performed in randomized order two HIIT sessions with either varied- or constant-intensity work intervals, matched for duration and mean power output. Acute physiological and perceptual responses were compared between HIIT sessions at the same time points.

Participants were instructed to refrain from all types of intense exercise 24 h before each laboratory visit and to prepare as they would for competition. They were instructed to consume identical meals 1 h before each laboratory visit and to refrain from caffeine during the preceding 3 h. All tests were performed free from distractions, under similar environmental conditions (16-17°C), with participants being cooled with a fan.

6.2.3 – Ergometer setup

All cyclists used the same bike (2017 Roubaix One.3 size 56, Fuji, Taichung, Taiwan) mounted on a cycle ergometer (KICKR, Wahoo Fitness, Atlanta, USA) considered to be valid and reliable (Zadow et al., 2016, Zadow et al., 2018). Saddle position was individually adjusted and measures were noted for replication. The bike was equipped with a crank-based power meter (SRAM S975, SRM, Jülich, Germany), from which power output and cadence were recorded. An indoor cycling training software (TrainerRoad v1.0.0.49262, TrainerRoad LLC, Reno, USA) was used to customize all testing sessions, which were performed in ergometer mode. The laptop was connected to the KICKR through Bluetooth and to the SRM through an ANT+ dongle. With this setup, the resistance of the KICKR was controlled by the power output and cadence readings of the SRM. Power output, cadence and HR were recorded by a cycle computer (PowerControl 8, SRM, Jülich, Germany) at a 1-Hz sampling rate and subsequently analysed using GoldenCheetah v3.4. The KICKR and the SRM were calibrated by the manufacturer prior to the study. Before each use, a member of the research team warmed up the KICKR by riding for 10 min at 100 W, and then performed the ‘spindown’ through the TrainerRoad software, which is a zero-offset calibration of the strain gauges based on bearing and belt friction. The zero-offset procedure of the SRM was performed according to the manufacturer’s recommendations.

To examine the validity of the power outputs generated by the KICKR through this setup, individual targets determined for each HIIT session (see text below) were compared to the SRM readings. A freely available spreadsheet (Hopkins, 2015) was used to assess data at 77%, 84% and 100% of maximal aerobic power (MAP) for agreement, with a total of 288, 96 and 288 duplicates, respectively. The comparison KICKR versus SRM revealed a typical error of estimate (TTE) of 7 W [CL: 6 – 7 W], correlation coefficient (r) of 0.98 [CL: 0.97 – 0.98] and mean bias of -3 W [CL: -4 – -3 W] at 77%MAP; a TEE of 2 W [CL: 2 – 3 W], r = 1.00 [CL: 1.00 – 1.00] and mean bias of 1 W [CL: 0 – 1 W] at 84%MAP; and a TEE of 8 W [CL: 7 – 9 W], r = 0.97 [CL: 0.97 – 0.98] and mean bias of 11 W [CL: 10 – 12 W] at 100%MAP. The ergometer setup was therefore deemed valid.

6.2.4 – Preliminary testing

In the first visit, participants' height and body mass were measured and they completed a cycling experience index questionnaire (Edwards et al., 2009), as well as standalone questions about their training habits. Briefly, by adding up the scores from each question, individuals are assigned a total score from 0 (representing a complete non-cyclist) to 37 (representing a highly experienced and well-trained cyclist) (Edwards et al., 2009). Participants subsequently completed a lactate threshold test, which started at 125 W, increasing by 50 W every fifth minute (25 W if blood lactate concentration [La^-] was ≥ 3 $mmol \cdot L^{-1}$), and terminated when [La^-] reached ≥ 4 $mmol \cdot L^{-1}$. Blood samples were taken from a fingertip at the last 30 s of each 5-min bout and were immediately analysed (Biosen C-Line, EKF Diagnostics, Penarth, UK). At the start of the test, cyclists chose their cadence, which they subsequently held constant throughout the remainder of the test. Power output at 4 $mmol \cdot L^{-1}$ [La^-] was calculated for each cyclist from the relationship between [La^-] and power output in the last two stages, by using linear regression. $\dot{V}O_2$ was measured during the last 3 min of each stage (15-s sampling time) using a computerised metabolic system with a mixing chamber (Oxycon Pro, Erich Jaeger, Hoechberg, Germany). Prior to every test, the gas analyser was calibrated with certified calibration gases of known concentrations and the flow turbine (Triple V, Erich Jaeger, Hoechberg, Germany) was calibrated with a 3 L syringe (5530 series, Hans Rudolph, Kansas City, USA).

After the lactate threshold test, cyclists rode for 10 min at a power output between 50 and 100 W before performing the maximal incremental test to determine both $\dot{V}O_{2max}$ and MAP. The test started at 200 W with work rate being increased by 25 W every minute until

voluntary exhaustion, or an inability to maintain cadence above 70 rev·min^{-1} despite verbal encouragement. Pedalling cadence was freely chosen but participants were instructed to avoid abrupt changes. $\dot{V}O_2$ was continually measured, and $\dot{V}O_{2max}$ was calculated as the highest 60-s mean. MAP was calculated according to Daniels (1985). This method extrapolates the relationship between submaximal power outputs and respective measures of $\dot{V}O_2$ to $\dot{V}O_{2max}$, by means of linear regression (Daniels, 1985). Power output data were recorded continuously throughout the test, with $\dot{W}_{max}$ calculated as the mean of the last 60 s of the incremental test. Immediately after the incremental test, a blood sample was taken from a fingertip and immediately analysed to establish [La^-]. Cyclists reported their peak RPE using Borg's 6-20 scale immediately after terminating the test.

6.2.5 – HIIT sessions

Initially, participants performed a 15-min warm-up based on Borg's 6-20 RPE scale. The warm-up consisted of 5 min at 11 (light), followed by three 1-min intervals at 16 (between hard and very hard), interspersed with two 2-min blocks, and a final 3 min, all at 9 (very light). Cyclists were allowed to manipulate the work rate imposed by the cycle ergometer in order to match the required RPE.

Both HIIT sessions started with 5 min at 50%MAP, followed by six 5-min work intervals at a mean intensity of 84%MAP, interspersed with 2.5-min recovery at 30%MAP. Varied-intensity work intervals consisted of three 30-s surges at 100%MAP, interspersed with two 1-min blocks, and a final 1.5 min at 77%MAP. Constant-intensity work intervals consisted of 5 min at 84%MAP. A detailed outline of the warm-up and both work intervals can be seen in Figure 6.1. The number of work intervals, their duration, and the duration of recovery intervals were chosen based on local athletes' perception of what constitutes a valuable training session for aerobic capacity development (i.e. anecdotal evidence). The mean intensity for the work intervals was chosen based on pilot testing to warrant both HIIT sessions would be completed with physiological responses typical of exercise performed within the severe intensity domain. As for the varied-intensity work intervals, the 30-s surges at 100%MAP were chosen based on previous work with cyclists (Rønnestad and Hansen, 2016) and cross-country skiers (Rønnestad et al., 2019). Given the superior time at >90%$\dot{V}O_{2max}$ elicited by 30-s compared to longer work intervals in the cycling study (Rønnestad and Hansen, 2016), it was reasoned that the 1.5 min at 100%MAP employed in

the cross-country skiing study (Rønnestad et al., 2019) could be split into three surges to characterize the varied-intensity work interval.

HR was continuously measured during the entire HIIT sessions. $\dot{V}O_2$ was measured during the 5-min work intervals (5-s sampling time) using the same equipment and following the calibration procedures adopted in the preliminary testing. Time at >90%$\dot{V}O_{2max}$ was calculated by summing all raw $\dot{V}O_2$ measures over the established cut-off. At the end of each work interval, fingertip blood samples were taken to assess [La^-], and RPE was recorded. Participants self-selected their cadence and water consumption was not restricted. Twenty minutes after finishing the HIIT sessions, sRPE was recorded. iTRIMP, a training-load metric based on HR (Manzi et al., 2009b), was also calculated to compare the training load between HIIT sessions. Within the iTRIMP calculation, exercise intensity is weighted according to participants' own HR–[La^-] exponential relationship (Manzi et al., 2009b), obtained during the preliminary testing. iTRIMP was calculated for each HIIT session by summing the weighted scores from every 5-s HR means (Manzi et al., 2009b).

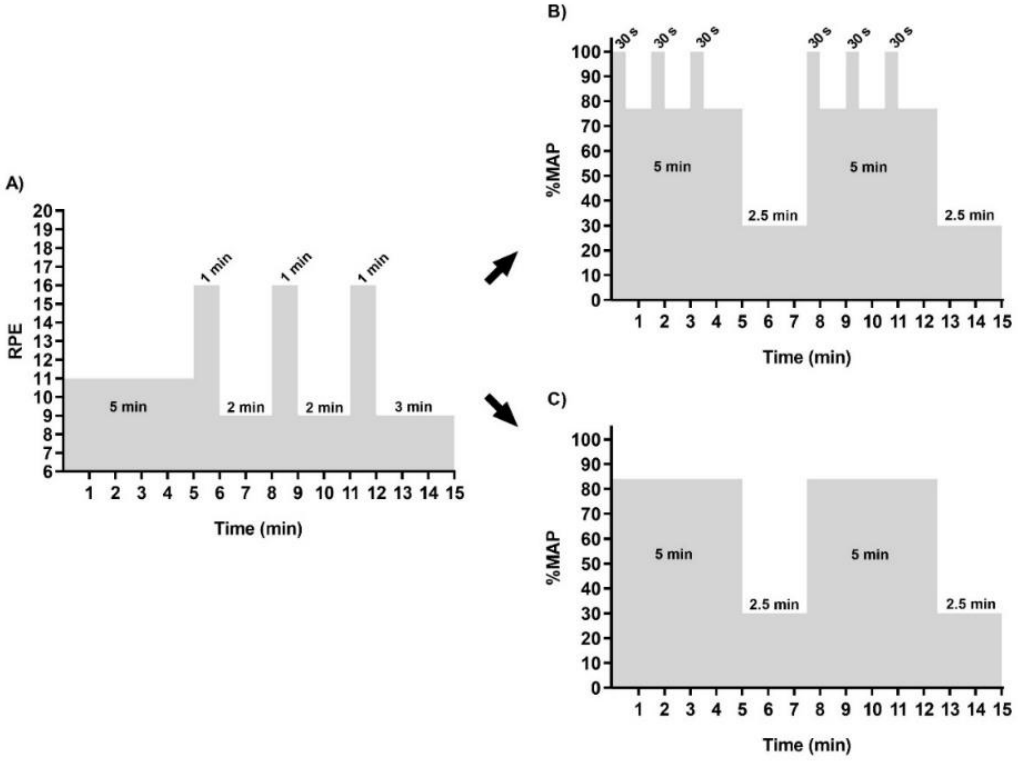

Figure 6.1 – Warm-up procedure based on ratings of perceived exertion (RPE) that was performed prior to both sessions of high-intensity interval training (panel A), varied-intensity work intervals (panel B), and constant-intensity work intervals (panel C). The intensity of both sessions was prescribed as a percentage of the individual's maximal aerobic power (MAP), and six work intervals were completed after 5 min at 50%MAP (which is omitted from the figure for clarity).

6.2.6 – Data analysis

Dependent variables were assessed for normality using Shapiro-Wilk tests and normal quantile plots. Paired t-tests were used to compare time at >90%$\dot{V}O_{2max}$, sRPE and iTRIMP between HIIT sessions. Two-way repeated measures analysis of variance (work interval mode x work interval number) were performed to test for differences in mean $\dot{V}O_2$ as %$\dot{V}O_{2max}$, total $\dot{V}O_2$, mean $\dot{V}E$, mean ventilatory equivalent for oxygen ($\dot{V}E \cdot \dot{V}O_2^{-1}$), mean f_R, mean tidal volume (V_T), mean $\dot{V}CO_2$, mean HR, [La^-], RPE, and mean cadence. Following analysis of variance, Bonferroni pairwise comparisons were used to identify where significant differences existed within the data. Cohen d or partial eta squared (η^2_p) were computed as effect size estimates. Absolute changes between HIIT sessions were calculated for mean $\dot{V}E$ ($\Delta\dot{V}E$) and total $\dot{V}O_2$ ($\Delta\dot{V}O_2$) per work interval. The association

between $\Delta\dot{V}E$ and $\Delta\dot{V}O_2$ was modelled by multilevel analysis with participant as a random effect (i.e. random intercept). A correlation coefficient (r) was then computed by adjusting for repeated observations within participants. Data were analysed using SSPS (SSPS Statistics 25, IBM, Armonk, USA) and significance level was set at $P \leq 0.05$. Results are presented as mean ± SD [90% confidence limits (CL)].

6.3 – Results

There was a longer time at >90%$\dot{V}O_{2max}$ for HIIT with varied- compared to constant-intensity work intervals (410 ± 207 versus 286 ± 162 s [CL: 312 – 508 versus 209 – 362 s]; t = 2.63; P = 0.02; d = 0.16 – Figure 6.2A), despite no difference in mean power output as measured by the SRM crank (324 ± 30 versus 323 ± 30 W [CL: 310 – 338 versus 309 – 337 W]; t = 1.35; P = 0.20; d = 0.01). There were also no differences in sRPE (6.0 ± 1.8 versus 6.6 ± 1.7 [CL: 5.2 – 6.9 versus 5.8 – 7.5]; t = -1.62; P = 0.13; d = -0.09 – Figure 6.2B), or iTRIMP (178 ± 43 versus 181 ± 46 [CL: 157 – 198 versus 160 – 203]; t = -0.43; P = 0.68; d = -0.02 – Figure 6.2C). The mean $\dot{V}O_2$ responses to both types of work intervals are presented in Figure 6.3.

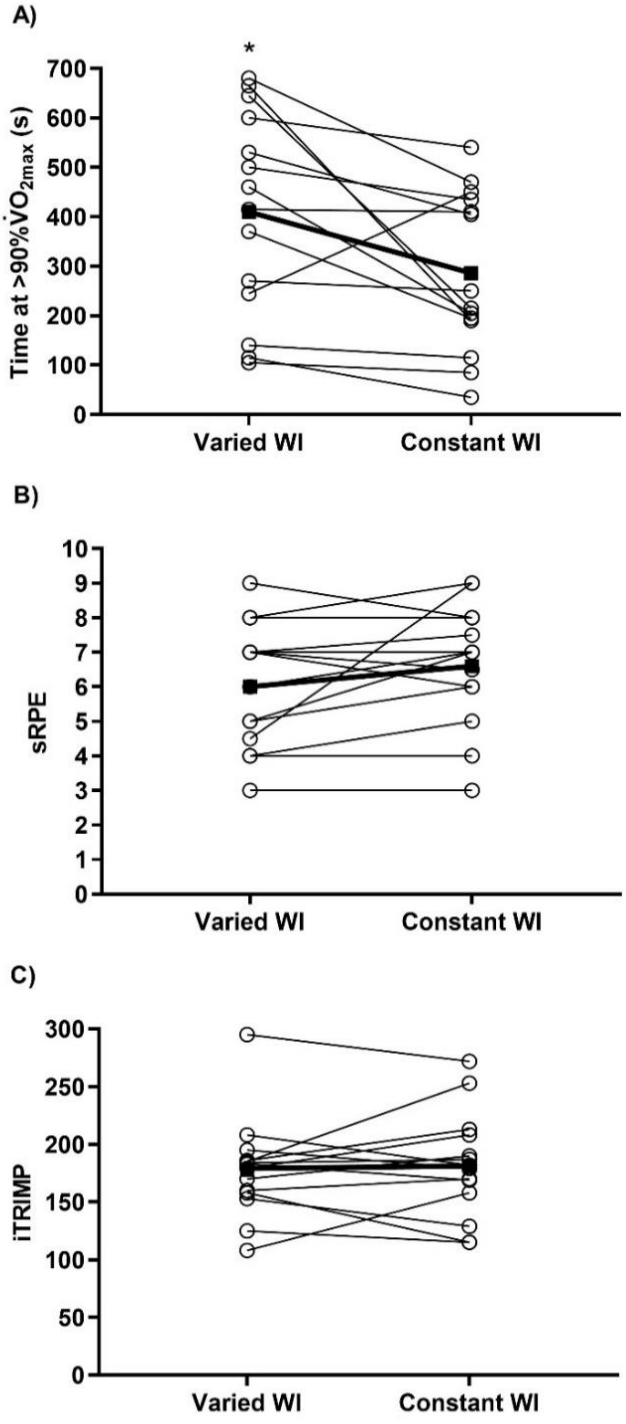

Figure 6.2 – Time spent above 90% of maximal oxygen uptake (time at >90%$\dot{V}O_{2max}$; panel A), session ratings of perceived exertion (sRPE; panel B), training load metric based on heart rate (iTRIMP; panel C). Open circles represent each participant and black squares represent the mean values for high-intensity interval training sessions with varied- (varied WI) and constant-intensity work intervals (constant WI). *Different from constant WI (P = 0.02).

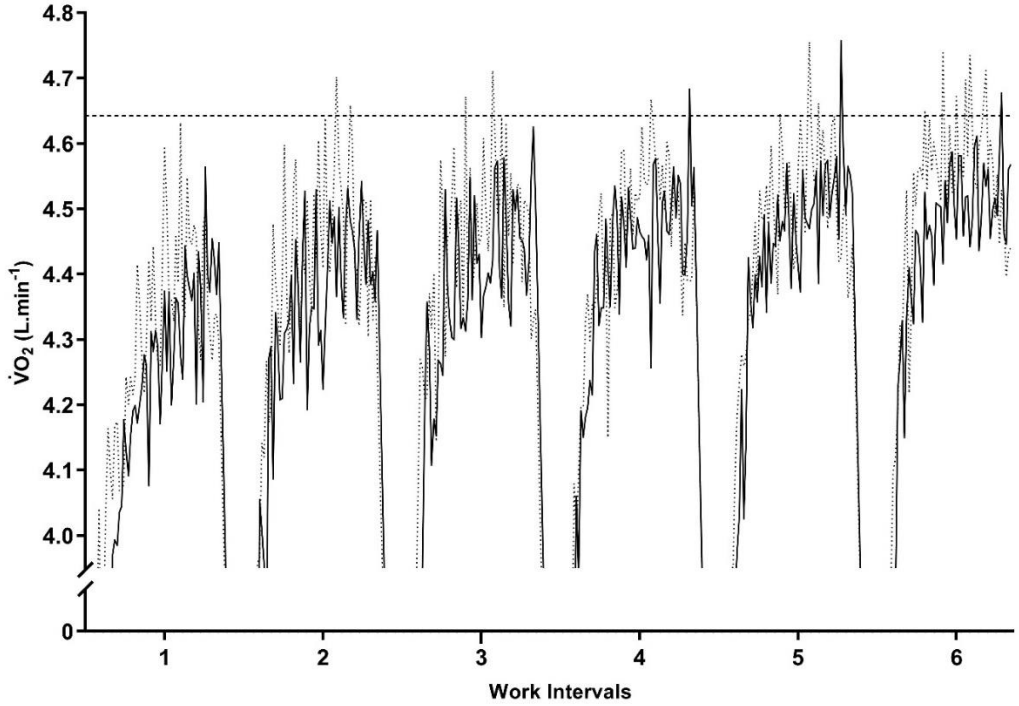

Figure 6.3 – Mean oxygen uptake ($\dot{V}O_2$) responses (5-s sampling time) to varied- (dotted line) and constant-intensity (solid line) work intervals. The horizontal dashed line represents 90% of maximal oxygen uptake (mean of all participants). SD is omitted from the figure for clarity. As individual participants reached 90% of maximal oxygen uptake at different time points, dotted and solid lines do not reflect the mean time spent over 90% of maximal oxygen uptake.

Statistics and effect size estimations from the analysis of variance are given in Table 6.2. No interactions between work interval mode and work interval number were found for $\%\dot{V}O_{2max}$ (Figure 6.4A), total $\dot{V}O_2$ (Figure 6.4B), $\dot{V}E$ (Figure 6.4C), $\dot{V}E \cdot \dot{V}O_2^{-1}$, f_R (Figure 6.4D), V_T (Figure 6.4E), $\dot{V}CO_2$ (Figure 6.4F), HR, $[La^-]$ (Figure 6.4G), RPE (Figure 6.4H), or cadence (Figure 6.4I). There was a main effect of work interval mode for $\%\dot{V}O_{2max}$, total $\dot{V}O_2$, $\dot{V}E$, $\dot{V}E \cdot \dot{V}O_2^{-1}$ and $\dot{V}CO_2$, but not for f_R, V_T, HR, $[La^-]$, RPE, or cadence. A main effect of work interval number was found for $\%\dot{V}O_{2max}$, total $\dot{V}O_2$, $\dot{V}E$, $\dot{V}E \cdot \dot{V}O_2^{-1}$, f_R, V_T, HR, $[La^-]$ and RPE. Pairwise comparisons revealed differences between consecutive work intervals for all variables (all $P \leq 0.05$), except for V_T, in which work interval 1 was different from 3, 4, 5 and 6 (all $P \leq 0.02$). There was no main effect of work interval number for $\dot{V}CO_2$ or cadence.

Table 6.2 – Statistics and effect size estimations from the analysis of variance for each variable analyzed.

	Interaction			Main effect of interval mode			Main effect of interval number		
	F	P	η_p^2	F	P	η_p^2	F	P	η_p^2
$\%\dot{V}O_{2max}$	1.03	0.39	0.07	11.26	0.005*	0.46	43.71	< 0.001*	0.77
Total $\dot{V}O_2$	1.00	0.40	0.07	10.78	0.006*	0.45	42.85	< 0.001*	0.77
$\dot{V}E$	0.32	0.76	0.02	8.42	0.01*	0.39	32.01	< 0.001*	0.71
$\dot{V}E \cdot \dot{V}O_2^{-1}$	0.61	0.56	0.05	5.65	0.03*	0.30	35.60	< 0.001*	0.73
f_R	0.55	0.59	0.04	3.50	0.08	0.21	41.79	< 0.001*	0.76
V_T	0.36	0.75	0.03	2.02	0.18	0.13	12.32	< 0.001*	0.49
$\dot{V}CO_2$	1.06	0.39	0.07	18.69	0.001*	0.59	2.38	0.09	0.15
HR	0.16	0.87	0.01	< 0.01	0.93	< 0.01	68.57	< 0.001*	0.85
$[La^-]$	0.50	0.58	0.04	1.54	0.24	0.11	35.75	< 0.001*	0.73
RPE	0.58	0.66	0.04	1.72	0.21	0.12	30.99	< 0.001*	0.70
Cadence	0.87	0.46	0.06	0.06	0.82	< 0.01	1.09	0.36	0.08

* Denotes statistical significance; $\%\dot{V}O_{2max}$: oxygen uptake as a percentage of maximal; Total $\dot{V}O_2$: total oxygen uptake; $\dot{V}E$: minute ventilation; $\dot{V}E \cdot \dot{V}O_2^{-1}$: ventilatory equivalent for oxygen; f_R: respiratory frequency; V_T: tidal volume; $\dot{V}CO_2$: carbon dioxide output; HR: heart rate; $[La^-]$: blood lactate concentration; RPE: ratings of perceived exertion.

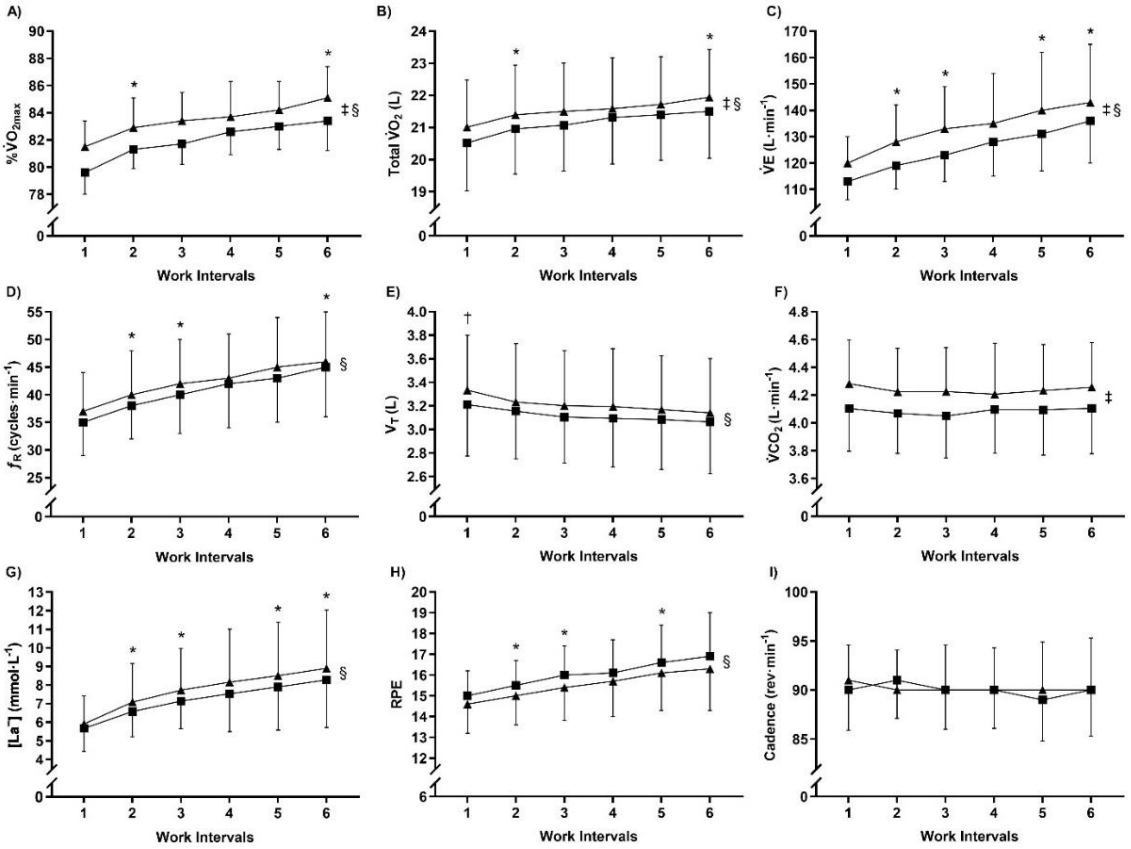

Figure 6.4 – Mean fraction of maximal oxygen uptake (%$\dot{V}O_{2max}$; panel A), total oxygen uptake (Total $\dot{V}O_2$; panel B), mean minute ventilation ($\dot{V}E$; panel C), mean respiratory frequency (f_R; panel D), mean tidal volume (V_T; panel E), mean carbon dioxide output ($\dot{V}CO_2$; panel F), blood lactate concentration ([La^-]; panel G), ratings of perceived exertion (RPE; panel H), and mean cadence (panel I). Data are displayed per work interval as mean ± SD for high-intensity interval training sessions with varied- (triangles) and constant-intensity work intervals (squares). *Different from previous work interval (all $P \leq 0.03$). †Different from work intervals 3, 4, 5 and 6 (all $P \leq 0.02$). ‡Main effect of work interval mode (all $P \leq 0.01$). §Main effect of work interval number (all $P < 0.001$).

The multilevel analysis produced the following model (y = mx + b):

$$\Delta\dot{V}O_2\,(ml) = 23.3 \cdot \Delta\dot{V}E\,(L \cdot min^{-1}) + 239.6 \quad (6.1)$$

(m_{SE} = 4.4; $P < 0.001$; b_{SE} = 118.9; P = 0.06; ICC = 0.43)

A moderate correlation was found between $\Delta\dot{V}E$ and $\Delta\dot{V}O_2$ ($r = 0.36$; $R^2 = 0.13$; $P = 0.002$).

6.4 – Discussion

Consistent with the first hypothesis, well-trained cyclists sustained higher %$\dot{V}O_{2max}$ when they performed the varied- compared to constant-intensity work intervals during a HIIT session. Time at >90%$\dot{V}O_{2max}$, %$\dot{V}O_{2max}$ sustained, and total $\dot{V}O_2$, all suggest an increased aerobic cost elicited by the varied-intensity work intervals. Importantly, this increased demand was not accompanied by a higher f_R, HR, [La^-], RPE, or cadence. Furthermore, no differences between conditions in sRPE or iTRIMP were found, which may suggest varied-intensity work intervals produce a higher training stimulus per dose of exercise. Consistent with the second hypothesis, $\dot{V}E$ was also higher during the varied- compared to constant-intensity work intervals. In addition, $\Delta\dot{V}E$ was moderately associated with $\Delta\dot{V}O_2$, suggesting differences in the oxygen cost of hyperpnoea partially explain the magnitude of $\dot{V}O_2$ differences between HIIT sessions.

Varying power output between 100% and 77%MAP within the work intervals of a HIIT session increased the mean time at >90%$\dot{V}O_{2max}$ by 43%, from 286 s (4 min 46 s) produced by the constant-intensity work intervals (84%MAP) to 410 s (6 min 50 s). This result stands out as the mean intensity and length of the work and recovery intervals as well as the total HIIT duration were not manipulated which often is the case in studies assessing time at or close to $\dot{V}O_{2max}$ (Billat, 2001, Buchheit and Laursen, 2013, Midgley and Mc Naughton, 2006, Rønnestad and Hansen, 2016, Turnes et al., 2016). Previously, Billat et al. (2013) demonstrated that effort could be minimized, and exercise sustained for more than 15 min at >95%$\dot{V}O_{2max}$, when power output was manipulated according to expired gas responses. Despite HIIT with varied-intensity work intervals producing a shorter duration at >90%$\dot{V}O_{2max}$ compared to that of Billat et al. (2013), the present results provide evidence for a more practical approach to programming this type of training.

Unique to the current study was that varied-intensity work intervals increased $\dot{V}O_2$ without affecting most variables reflecting the physiological and perceptual strain of exercise. In contrast, Zadow et al. (2015) reported times at >85%$\dot{V}O_{2max}$ of 2 min 31 s and 2 min 04 s, for respectively all-out and constant-intensity work intervals, but with greater HR, RPE, and sRPE (Zadow et al., 2015). Collectively, these results suggest there may be a tolerance limit for the magnitude of power output variation that allows cyclists to optimize time at >90%$\dot{V}O_{2max}$ without compromising exercise capacity. Another strength of the present work is that HIIT sessions were matched for all prescription elements affecting the exercise dose,

except power output distribution. For instance, Lisbôa et al. (2015) reported longer time at >90%$\dot{V}O_{2max}$ (4 min 19 s versus 2 min 03 s) following decreasing- versus constant-intensity work intervals, but conditions were matched by participant's W' (Lisbôa et al., 2015). Work and recovery interval durations were not controlled, potentially affecting time at a high %$\dot{V}O_{2max}$ more than the power output distribution itself (Billat, 2001, Buchheit and Laursen, 2013, Midgley and Mc Naughton, 2006, Rønnestad and Hansen, 2016, Turnes et al., 2016). Thus, the higher time at >90%$\dot{V}O_{2max}$ was likely achieved by a change in exercise dose.

HIIT can be prescribed in different formats according to the aim of the training session. To produce the longest times at or close to $\dot{V}O_{2max}$, short work intervals (< 1 min) have been recommended (Billat, 2001, Buchheit and Laursen, 2013, Midgley and Mc Naughton, 2006, Rønnestad and Hansen, 2016, Turnes et al., 2016). In agreement with this proposition, adding repeated power output variations within longer 5-min work intervals increased time at >90%$\dot{V}O_{2max}$. Nevertheless, there is contrasting evidence from training studies, with evidence that both short (Rønnestad et al., 2015, Turnes et al., 2016) and long work intervals (Bacon et al., 2013, Seiler et al., 2013) may trigger a potent stimulus for increasing $\dot{V}O_{2max}$. This suggests time at >90%$\dot{V}O_{2max}$ is unlikely to be the only training variable driving $\dot{V}O_{2max}$ enhancements. Its relatively poor reliability must also be taken into account (Midgley et al., 2007). Despite these considerations, it can be speculated that the novel HIIT session, if repeated over time, may combine the benefits of both short and longer work intervals. Further work is necessary to confirm this hypothesis.

Ventilatory responses to work intervals of different power output distributions have been previously neglected (Lisbôa et al., 2015, Zadow et al., 2015). Interestingly, the present results suggest they play a role in the observed changes in total $\dot{V}O_2$. Compared to constant-intensity work intervals, varied intensity produced higher $\dot{V}E$ and $\dot{V}E \cdot \dot{V}O_2^{-1}$, implying a greater mechanical work of the pulmonary system and an increased oxygen cost of hyperpnoea (Aaron et al., 1992a, Aaron et al., 1992b, Dominelli et al., 2015). Indeed, the multilevel analysis used in this study predicted that for each L of increase in $\dot{V}E$, $\dot{V}O_2$ is increased by 4.7 ml. This is nevertheless higher than the cost of exercise hyperpnoea reported by Aaron et al. (1992a) as 2.9 ml of oxygen per L of $\dot{V}E$, or more recently by Dominelli et al. (2015) as 2.4 $ml \cdot L^{-1}$. Taking together the model intercept of 239.6 ml, results suggest mechanisms other than an increased $\dot{V}E$ may account to a greater extent for the observed

changes in aerobic cost of HIIT. It is therefore not surprising that only a moderate correlation between $\Delta\dot{V}E$ and $\Delta\dot{V}O_2$ ($r = 0.36$) was found in the present study.

The fact that no differences in f_R or V_T were found between varied- and constant-intensity work intervals, alongside the differences in $\dot{V}E$, has some practical and mechanistic implications. Practically, f_R has been considered a marker of physical effort (Nicolò et al., 2017b), reinforcing the sense of equivalence in strain levels between both types of HIIT. Mechanistically, a higher $\dot{V}E$ with no significant changes in either f_R or V_T indicates that both contributed to the increases in $\dot{V}E$, although in small magnitudes or with inter-individual differences, challenging the hypothesis of a distinct mechanistic control of f_R and V_T during exercise (Nicolò et al., 2017b). Indeed, it has been previously suggested that during high-intensity exercise central command regulates $\dot{V}E$ preferentially through changes in f_R (Nicolò et al., 2017b), which the present data do not support. Instead, Tipton et al. (2017) have proposed $\dot{V}E$ is regulated by a complex integration of mechanical and physiological factors, making it difficult to completely associate f_R and V_T with a particular type of reflex. Therefore, the higher $\dot{V}E$ in the varied- compared to the constant-intensity work intervals is likely the result of a tightly coupled interaction between the increases in f_R and V_T that manifest during this type of exercise.

Additional mechanistic insight can be gained from a close inspection of Figure 6.3. Repeated surges at 100%MAP, as opposed to a single surge at the start of each work interval, seem required to produce the observed differences in time at >90%$\dot{V}O_{2max}$. Not only the oxygen cost of hyperpnoea, but also the oxygen cost of muscle contraction, may have been greater during the varied- compared to the constant-intensity work intervals. Higher exercise intensities have been shown to elicit a more uniform activation of the quadriceps femoris muscles (Heinonen et al., 2012) and their motor units (Heinonen et al., 2012, Hodson-Tole and Wakeling, 2009). Thus, it is reasonable to assume some high-threshold fibres were only recruited at 100%MAP. The low efficiency and high fatigability of these fibres may have contributed to an increased whole-body $\dot{V}O_2$ and time at >90%$\dot{V}O_{2max}$ (Jones et al., 2011). Besides, the $\dot{V}O_2$ kinetics hypothesis, as proposed by other authors (Bailey et al., 2011, Jones et al., 2008b, Lisbôa et al., 2015, Zadow et al., 2015), cannot be discarded. If the initial 30-s surges of the varied-intensity work intervals did not directly affect time at >90%$\dot{V}O_{2max}$, faster $\dot{V}O_2$ kinetics apparently contributed to a higher %$\dot{V}O_{2max}$ sustained and total $\dot{V}O_2$.

Future studies should use breath-by-breath ergospirometry and leg electromyography to provide evidence for these hypotheses.

To summarise, in comparison to a HIIT session with constant-intensity work intervals, well-trained cyclists sustain higher $\%\dot{V}O_{2max}$ when power output is repeatedly varied within the work intervals. This effect is partially mediated by an increased oxygen cost of hyperpnoea. Well-trained cyclists looking for alternative strategies to optimize training stimulus are advised to try the varied-intensity work intervals as outlined here. Whether performance adaptations will be superior to constant-intensity work intervals remains to be established by a longitudinal study; but similar f_R, HR, $[La^-]$, RPE and training load metrics suggest it is unlikely that negative training outcomes occur.

Chapter 7 – Modelling inter-individual variability in acute and adaptive responses to interval training - insights into exercise intensity normalisation

7.1 – Introduction

It is commonly believed that the magnitude of physiological adaptations varies between individuals undertaking the same exercise training programme (Astorino et al., 2018, Bonafiglia et al., 2019b, Bouchard et al., 1999, Coakley and Passfield, 2018b, Del Giudice et al., 2020, Hecksteden et al., 2018b, McLellan and Skinner, 1981, Montero and Lundby, 2017, Preobrazenski et al., 2019, Vollaard et al., 2009, Weatherwax et al., 2019). A major factor behind this phenomenon is suggested to be genetics (Mann et al., 2014), which is believed to account for approximately 50% of the changes in $\dot{V}O_{2max}$ (Bouchard et al., 1999, Bouchard et al., 2011). Even though genetics may play a role in the magnitude of adaptive responses, it has been proposed that methods of exercise intensity normalisation in experimental studies do not provide comparable metabolic stress across participants (Iannetta et al., 2020, Jamnick et al., 2020, Mann et al., 2013, Vollaard et al., 2009), contributing to variability in the extent to which training adaptations occur (Mann et al., 2014). As a proof of this concept, when exercise intensity is normalised as $\%HR_{max}$, a method with recognised limitations (Iannetta et al., 2020, Jamnick et al., 2020, Katch et al., 1978, Mann et al., 2013), $\dot{V}O_{2max}$ changes following two identical training interventions separated by a washout are only moderately correlated ($r = 0.31$) (Del Giudice et al., 2020). Accordingly, a necessary step to understanding adaptive response heterogeneity is to refine the scientific basis of exercise intensity prescription.

The optimal method for exercise intensity normalisation may be dependent on population of interest, intensity domain of training (i.e. moderate, heavy, very heavy, or severe (Rossiter, 2011)), and exercise pattern (i.e. continuous or intermittent) (Jamnick et al., 2020, Mann et al., 2013). Indeed, there have been contrasting reports on whether some intensity prescription methods could minimize adaptive variability (McLellan and Skinner, 1981, Preobrazenski et al., 2019, Weatherwax et al., 2019). To study this, typically, two groups undertake the same training programme, but with different exercise-intensity normalisation methods used to select individual work rate targets for training (McLellan and Skinner, 1981, Preobrazenski et al., 2019, Weatherwax et al., 2019). In this respect, Weatherwax et al. (2019) concluded that less inter-individual variability in $\dot{V}O_{2max}$ adaptive responses was elicited when comparing a prescription that accounts for exercise intensity domains with one that does not, although, by contrast, McLellan and Skinner (1981) reported no differences. Furthermore, Preobrazenski et al. (2019) showed no differences in the magnitude of inter-individual variability of several adaptive responses, including $\dot{V}O_{2max}$, when prescriptions

based on the maximal work rate from an incremental test (%$\dot{W}_{max}$) and the talk test were compared (see Reed and Pipe (2014) for talk test details). However, Preobrazenski et al. (2019) also found that the mean [La^-] of the first training session was positively associated with $\dot{V}O_{2max}$ changes within the $\dot{W}_{max}$ group, providing some evidence that individuals experiencing larger metabolic stress may also experience larger adaptive response (and vice versa) (Mann et al., 2013, Mann et al., 2014). Collectively, the inconsistency of these findings indicates that further research is required to ascertain the extent to which exercise-intensity normalisation affects adaptive response variability, and in which contexts.

Interestingly, Montero and Lundby (2017) have demonstrated that maximising training dose is necessary to ensure all individuals within a study cohort improve $\dot{W}_{max}$ and $\dot{V}O_{2max}$. This finding suggests that McLellan and Skinner (1981) and Preobrazenski et al. (2019) may have failed to provide their participants with sufficient training-induced stress, making it difficult to untangle potential between-group differences in adaptive variability (Joyner and Lundby, 2018). The only study investigating exercise intensity normalisation that assessed adaptive response heterogeneity of a HIIT intervention compared results with the available literature as opposed to a comparative group (Astorino et al., 2018), hampering interpretation of their findings. Hence, more studies are required to shed light on this topic.

For intensive training, maximal self-paced intervals have often been employed as a method of exercise intensity normalisation, both in cross-sectional (Brosnan et al., 2000, Nicolò et al., 2014, Villerius et al., 2008) and longitudinal interventions (Rønnestad et al., 2020, Seiler et al., 2013, Seiler and Sylta, 2017). Frequently described as "how elite athletes train" (Brosnan et al., 2000, Nicolò et al., 2014, Rønnestad et al., 2020, Seiler et al., 2013, Seiler and Sylta, 2017, Villerius et al., 2008), this approach is based on the premise that there exists an individualised maximal sustainable work rate for a given HIIT format. As long as work intervals are performed within the very heavy intensity domain, this concept has precedents in the hyperbolic relationship between work rate and TTE (Ferguson et al., 2013, Jones and Vanhatalo, 2017). Surprisingly, there have been no attempts to assess the effectiveness of this method of intensity normalisation in comparison with other approaches such as %$\dot{W}_{max}$.

In the present study, it was investigated the inter-individual variability in acute and chronic (i.e. adaptive) responses to a training programme in two groups of cyclists. It was hypothesised that the group in which training intensity was prescribed relative to the

maximal sustainable work rate in a self-paced HIIT session ($\dot{W}_{max\text{-}SP}$) would exhibit less inter-individual variability in acute exercise responses, leading to less variability in adaptive responses, compared with the group in which training intensity was prescribed as $\%\dot{W}_{max}$. It was also hypothesised that the $\%\dot{W}_{max}$ group would demonstrate a higher proportion of unfinished training sessions, due to miscalculated work rate targets leading to premature exhaustion, potentially compromising the group's average adaptive responses.

7.2 – Methods

7.2.1 – Participants

Nineteen recreationally trained cyclists (age: 36 ± 10 years, height: 179 ± 8 cm, body mass: 76.3 ± 8.6 kg, $\dot{V}O_{2max}$: 54 ± 6 $ml \cdot kg^{-1} \cdot min^{-1}$) volunteered for this study. Ethical standards compliance is detailed in Chapter 3 – General methods.

7.2.2 – Study design

Participants were involved in this study for 16 weeks (see Table 7.1), with weeks designated for testing (4 weeks), control (6 weeks) and training intervention (6 weeks). While distinct methods of exercise intensity prescription were used for each group during the training intervention, testing and control phases consisted of identical requirements for all participants. Testing before and after the control phase served as a control against which to gauge the effects of the training interventions (Voisin et al., 2019). Moreover, the testing phase halfway through the training intervention at week 11 enabled the estimation of inter-individual variability in adaptive responses without the need for repeating the training intervention (Hecksteden et al., 2018b). This experimental design makes it possible to estimate inter-individual variability in adaptive responses devoid of intra-individual variability (Hecksteden et al., 2018b, Voisin et al., 2019).

Table 7.1 – Timeline of the study.

Week	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Phase	Testing			Control				Testing	Training Intervention ($\%\dot{W}_{max}$) / Training Intervention ($\%\dot{W}_{max-SP}$)			Testing	Training Intervention ($\%\dot{W}_{max}$) / Training Intervention ($\%\dot{W}_{max-SP}$)			Testing
Laboratory Visits	3			N/A				3	2	2	2	3	2	2	2	3

$\%\dot{W}_{max}$, group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test; $\%\dot{W}_{max-SP}$, group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session; N/A, not applicable.

7.2.3 – Testing phase

At approximately the same time of the day, participants visited the laboratory three times per week, at least 48 h apart. In both the first and second visits, participants were weighed and completed a lactate threshold test and an incremental test to exhaustion (i.e. duplicate measures were averaged to improve reliability; see Table 7.2). In the third visit, participants performed a self-paced HIIT session. Common testing procedures are outlined in Chapter 3 – General methods.

Table 7.2 – Day-to-day reliability estimates for each testing week.

Measure	$\dot{V}O_{2max}$ (L·min^{-1})				$\dot{W}_{max}$ (W)				4 mmol·L$^{-1}_{PO}$ (W)				GE (%)			
Week	0	7	11	15	0	7	11	15	0	7	11	15	0	7	11	15
Typical Error	0.115	0.145	0.115	0.130	9	5	10	4	7	7	8	6	0.7	0.7	0.6	0.8
CV (%)	2.9	3.7	2.7	3.1	2.4	1.2	2.9	1.1	3.1	2.7	3.7	2.7	3.9	3.5	3.1	4.0
ICC	0.96	0.93	0.97	0.96	0.95	0.99	0.95	0.99	0.97	0.98	0.96	0.98	0.87	0.83	0.81	0.83

CV, coefficient of variation; ICC, intraclass correlation coefficient; $\dot{V}O_{2max}$, maximal oxygen uptake; $\dot{W}_{max}$, maximal work rate in an incremental test; 4 mmol·L$^{-1}_{PO}$, power output associated with 4 mmol·L^{-1} blood lactate concentration; GE, gross efficiency. A freely available spreadsheet was used to calculate reliability estimates (Hopkins, 2015).

The lactate threshold test started at 100 W, increasing by 50 W every fifth minute (or 25 W if [La^-] was ≥ 2.5 mmol·L^{-1}), and terminating when [La^-] reached ≥ 4 mmol·L^{-1}. Blood samples taken from a fingertip (at the last 30 s of each 5-min bout) were immediately analysed for [La^-]. Power output associated with 4 mmol·L^{-1} [La^-] was calculated for each cyclist from the relationship between [La^-] and power output in the last two stages. Before the start, participants chose their preferred cadence for the entire test (91 ± 4 rev·min^{-1}). Both the work rates and cadence of the first lactate threshold test were held constant throughout the study. Breath-by-breath gas exchange was monitored throughout the test and subsequently smoothed to 30-s averages. Gross efficiency, measured as the ratio between power output and energy expenditure (Hopker et al., 2009), was calculated at 150 W from the mean gas exchanges in the last 2.5 min of the stage. Energy expenditure was estimated assuming negligible protein oxidation according with the equations of Péronnet and Massicotte (1991). All participants met the criterion of a respiratory exchange ratio ≤ 1.0 in all tests.

After the lactate threshold test, participants cycled for 10 min at a power output between 50 and 100 W. Subsequently, completed an incremental test (see Chapter 3 – General methods for details).

The self-paced HIIT session consisted of six 4-min work intervals interspersed with 2-min active recovery. Participants started immediately after a 10-min warm-up at power outputs between 100 and 150 W. They were required to produce the highest possible amount of work to establish $\dot{W}_{max\text{-}SP}$ (i.e. highest possible mean power output across all six work intervals) and received instructions to keep power constant between and within work intervals. Recovery intervals had to be performed at power outputs ≤ 70 W. HR was recorded as the last-minute average of each work interval. RPE was noted immediately after each work interval.

7.2.4 – Control phase

During this phase, participants did not attend the laboratory. However, they were required to keep their weekly training duration similar to the last two weeks before joining the study, and to avoid structured high-intensity training.

7.2.5 – Training intervention phase

Due to the relatively small number of participants recruited for this study, the first was truly randomised, with subsequent participants allocated to one of the two training interventions to keep groups closely matched with regard to dependent variables; i.e. minimization approach (Hecksteden et al., 2018a). Participants were not aware of the group to which they were assigned. In other words, they were blinded as to the methods of exercise intensity normalisation used in this study. Participants of both groups attended the laboratory twice per week, at least 72 h apart, to perform HIIT sessions consisting of 4-min work intervals interspersed with 2-min active recovery, at predefined work rates. Six training sessions were performed from weeks 8 to 10, and another six from weeks 12 to 14. While in one training intervention (%$\dot{W}_{max}$), the work intervals were performed at 80%$\dot{W}_{max}$ measured on the first incremental test (i.e. visit one of testing; see Table 7.1); in the other (%$\dot{W}_{max\text{-}SP}$), the work intervals were performed at 100%$\dot{W}_{max\text{-}SP}$. Recovery intervals were performed at 20% of the work rate prescribed for the work intervals, irrespective of which training intervention were participants allocated; i.e. 0.2·(mean$_{[80\%\dot{W}max,\ 100\%\dot{W}max\text{-}SP]}$). Participants of both groups were prescribed six work intervals in each training session, except for weeks 8 and 12, in which five work intervals were prescribed to boost their confidence that sessions could be completed. Even though they were always strongly encouraged, voluntary exhaustion or inability to maintain cadence above 70 rev·min^{-1} were utilised as criteria to establish individual completion rates in the event of premature termination. Cadence was recorded as the average of each work interval (or the average of completed duration in case of exhaustion), and HR as the last-minute average of each work interval (or the average of completed duration if shorter than one minute). RPE was noted immediately after each work interval or at exhaustion. All HIIT sessions commenced with a 15-min warm-up and finish with a 3-min cool-down, at respectively 60% and 40% of the work rate prescribed for the work intervals, irrespective of which training intervention were participants allocated; i.e. 0.6·(mean$_{[80\%\dot{W}max,\ 100\%\dot{W}max\text{-}SP]}$), and 0.4·(mean$_{[80\%\dot{W}max,\ 100\%\dot{W}max\text{-}SP]}$). As $\dot{V}O_{2max}$ gains have been shown to plateau after 3 weeks of high-intensity training at the same work rates (Hickson et al., 1981), training targets were re-adjusted following the testing phase of week 11, no matter if participants exhibited an increase or a decrease in performance. Participants were instructed to perform their remaining training sessions (i.e. outside the laboratory) at work rates below the power output associated with 4 mmol·L^{-1} [La^{-}], and to keep weekly training duration similar to the control phase.

7.2.6 – Training intensity determination

To ensure that HIIT intensity was comparable on average, the percentage of each prescription benchmark (i.e. 80%$\dot{W}_{max}$ and 100%$\dot{W}_{max\text{-}SP}$) was derived based on pilot work with an independent sample of three male and one female cyclists (age: 26 ± 4 years, height: 176 ± 12 cm, body mass: 72.8 ± 15.0 kg, $\dot{V}O_{2max}$: 55 ± 5 ml·kg^{-1}·min^{-1}). They performed two incremental tests to exhaustion and two self-paced HIIT sessions. The averaged work rates for 80%$\dot{W}_{max}$ and 100%$\dot{W}_{max\text{-}SP}$ corresponded to 3.59 ± 0.29 and 3.56 ± 0.41 W·kg^{-1}, respectively (P = 0.705).

7.2.7 – Data analysis

Data were assessed for normality using Shapiro-Wilk's test and normal quantile plots. To investigate between-group differences in target work rates for the training sessions, independent samples t-tests were used. Training intervention completion rates were assessed for a between-group difference using a Mann-Whitney test. Training RPE, HR, and cadence were investigated via linear mixed models with participant as a random effect, and group, training session, and work interval as fixed effects. To identify evidence of between-group differences in the magnitude of inter- and intra-individual variability, models were fitted with homogeneous and heterogeneous inter- and intra-individual variance structures for group.

To investigate between-group differences in the adaptive response variables (i.e. $\dot{V}O_{2max}$, $\dot{W}_{max}$, power output associated with 4 mmol·L^{-1} [La^{-}], gross efficiency, $\dot{W}_{max\text{-}SP}$, and body mass) prior to the intervention, independent samples t-tests were used. Differences in adaptive response variables between testing weeks 0, 7, 11, and 15 were assessed using repeated-measures analysis of variance, with Bonferroni pairwise comparisons used to identify where significant differences existed within the data. Linear mixed models, with participant as a random effect, and group and testing occasion as fixed effects, were used to test for a group effect on adaptive response variables' change from week 0 while controlling for their absolute baseline scores. To investigate inter-individual variability in adaptive responses to training, piecewise linear mixed models were used with participant and participant-by-intervention week interaction as random effects, and control week and intervention week as fixed effects. The standard error of the participant-by-intervention week interaction was used to calculate confidence intervals associated with individual adaptive responses. Individuals whose confidence intervals overlapped 0 were considered

non-responders, whereas those whose confidence intervals did not overlap 0 were considered responders or adverse responders based on a positive or negative response, respectively. Optimal model fit was determined based on likelihood ratio tests. Pearson's correlation was employed to examine the relationship between modelled adaptive responses.

Data were analysed using Prism 8 (GraphPad, San Diego, USA), with model fitting performed in R 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria). Significance level was set at $P \leq 0.05$, and confidence level was set at 95%. Results are presented as mean ± SD unless otherwise stated. To aid understanding of results, the reader unfamiliarised with linear mixed models is referred to Brown (2021) for a tutorial.

7.3 – Results

7.3.1 – Training intervention

All participants attended all sessions of the training intervention. Target work rates for training are presented in Table 7.3. No between-group differences were detected for any of the target work rates, at either the first or second half of the training intervention (all $P \geq 0.220$). Training intervention completion rates are presented in Table 7.4. Due to premature exhaustion, participants of the $\%\dot{W}_{max}$ group did not complete the entire sessions as often as participants of the $\%\dot{W}_{max\text{-}SP}$ group, resulting in a lower overall completion rate.

Table 7.3 – Target work rates for training ($W \cdot kg^{-1}$).

Group	Training Intervention (1st half)				Training Intervention (2nd half)			
	Warm-up	Work Intervals	Recovery Intervals	Cool-down	Warm-up	Work Intervals	Recovery Intervals	Cool-down
$\%\dot{W}_{max}$	2.30 ± 0.21	3.89 ± 0.35	0.77 ± 0.07	1.53 ± 0.14	2.35 ± 0.21	3.97 ± 0.36	0.78 ± 0.07	1.57 ± 0.14
$\%\dot{W}_{max\text{-}SP}$	2.26 ± 0.17	3.76 ± 0.32	0.75 ± 0.06	1.51 ± 0.11	2.29 ± 0.17	3.77 ± 0.32	0.76 ± 0.06	1.53 ± 0.11

$\%\dot{W}_{max}$, group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test; $\%\dot{W}_{max\text{-}SP}$, group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session.

Table 7.4 – Training intervention completion rates (%).

Training	Participants ($\%\dot{W}_{max}$)										Participants ($\%\dot{W}_{max-SP}$)								
Session	1	3	5	7	9	11	13	15	17	19	2	4	6	8	10	12	14	16	18
1	100.0	100.0	100.0	100.0	68.0	100.0	66.0	50.0	100.0	100.0	86.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
2	88.0	100.0	100.0	100.0	100.0	100.0	100.0	64.0	100.0	68.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
3	88.3	100.0	76.7	100.0	71.7	100.0	88.3	40.0	55.0	56.7	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
4	100.0	100.0	71.7	100.0	100.0	100.0	66.7	75.0	100.0	55.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
5	100.0	100.0	100.0	100.0	100.0	100.0	88.3	53.3	100.0	55.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
6	100.0	100.0	66.7	100.0	100.0	100.0	100.0	73.3	100.0	58.3	91.7	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
7	100.0	84.0	80.0	100.0	100.0	100.0	70.0	50.0	100.0	100.0	88.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
8	100.0	68.0	86.0	100.0	100.0	100.0	86.0	50.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
9	60.0	73.3	73.3	100.0	100.0	100.0	53.3	60.0	100.0	100.0	91.7	71.7	100.0	100.0	100.0	100.0	100.0	100.0	100.0
10	90.0	88.3	53.3	100.0	100.0	85.0	86.7	40.0	100.0	100.0	93.3	100.0	100.0	100.0	70.0	100.0	100.0	100.0	100.0
11	50.0	73.3	90.0	100.0	100.0	68.3	73.3	41.7	100.0	100.0	73.3	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
12	100.0	71.7	88.3	100.0	100.0	53.3	91.7	41.7	100.0	100.0	56.7	71.7	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Overall	89.3	88.2	81.6	100.0	95.1	91.8	80.9	53.2	96.0	82.2	89.9	95.0	100.0	100.0	97.4	100.0	100.0	100.0	100.0
Group Median [Q1 - Q3]	88.8 [81.4 - 95.3]										100.0 [96.2 - 100.0] *								

$\%\dot{W}_{max}$, group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test; $\%\dot{W}_{max-SP}$, group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session; Q1, 25th percentile; Q3, 75th percentile. * denotes significant difference (P = 0.003).

There were no between-group differences for RPE, HR, or cadence (see $\%\dot{W}_{max\text{-}SP}$ estimates in Table 7.5), and there was no evidence of between-group differences in the magnitude of inter-individual variability for these variables (Table 7.6). In contrast, there was evidence of lower intra-individual variability in acute training responses for the $\%\dot{W}_{max\text{-}SP}$ group (Table 7.6).

Table 7.5 – Linear mixed model estimates.

Random Effects (SD)									
	RPE			Heart Rate (beats·min^{-1})			Cadence (rev·min^{-1})		
Intercept	0.8			9			6		
Residual	0.8			3			3		
Fixed Effects									
	RPE			Heart Rate (beats·min^{-1})			Cadence (rev·min^{-1})		
	Estimate	SE	P	Estimate	SE	P	Estimate	SE	P
Intercept	15.4	0.3	< 0.001	173	3	< 0.001	96	2	< 0.001
$\%\dot{W}_{max\text{-}SP}$	-0.5	0.4	0.204	-7	4	0.089	0	3	0.988
Training Session 2	-0.2	0.1	0.061	-1	1	0.108	1	1	0.146
Training Session 3	-0.5	0.1	< 0.001	-1	1	0.009	1	1	0.054
Training Session 4	-0.4	0.1	0.001	0	1	0.989	2	1	0.004
Training Session 5	-0.5	0.1	< 0.001	-2	1	< 0.001	0	1	0.399
Training Session 6	-0.7	0.1	< 0.001	-1	1	0.075	3	1	< 0.001
Training Session 7	-0.3	0.1	0.013	1	1	0.056	2	1	0.001
Training Session 8	-0.3	0.1	0.033	1	1	0.013	2	1	< 0.001
Training Session 9	-0.5	0.1	< 0.001	1	1	0.131	1	1	0.023
Training Session 10	-0.6	0.1	< 0.001	1	1	0.108	2	1	< 0.001
Training Session 11	-0.5	0.1	< 0.001	1	1	0.044	2	1	0.006
Training Session 12	-0.6	0.1	< 0.001	2	1	0.002	2	1	< 0.001
Work Interval 2	1.2	0.1	< 0.001	4	0	< 0.001	0	0	0.376
Work Interval 3	2.4	0.1	< 0.001	6	0	< 0.001	0	0	0.232
Work Interval 4	3.3	0.1	< 0.001	8	0	< 0.001	-1	0	0.002
Work Interval 5	4.1	0.1	< 0.001	9	0	< 0.001	-1	0	< 0.001
Work Interval 6	4.6	0.1	< 0.001	9	0	< 0.001	-1	0	0.009

Formula: dependent variable = intercept + group estimate + training session estimate + work interval estimate. For $\%\dot{W}_{max}$, training session 1, and work interval 1, consider an estimate of 0. $\%\dot{W}_{max}$, group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test; $\%\dot{W}_{max\text{-}SP}$, group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session; RPE, ratings of perceived exertion.

Table 7.6 – Variability in acute exercise responses (SD).

	Inter-individual variability			Intra-individual variability		
	$\%\dot{W}_{max}$	$\%\dot{W}_{max\text{-}SP}$	P	$\%\dot{W}_{max}$	$\%\dot{W}_{max\text{-}SP}$	P
RPE	0.9	0.7	0.360	0.9	0.8	0.005
Heart Rate (beats·min^{-1})	9	8	0.915	4	3	< 0.001
Cadence (rev·min^{-1})	6	5	0.534	5	3	< 0.001

$\%\dot{W}_{max}$, group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test; $\%\dot{W}_{max\text{-}SP}$, group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session; RPE, ratings of perceived exertion.

7.3.2 – Training outcomes

Participants attended all testing sessions, except for one participant of the $\%\dot{W}_{max\text{-}SP}$ group that did not attend the second visit of week 0. No between-group differences were detected for any of the adaptive response variables, at either week 0 or week 7 (all $P \geq 0.233$), suggesting the participant allocation into groups was successful. During the self-paced HIIT session, RPEs associated with each work interval were not different between weeks (all $P \geq 0.102$). This is despite an increased HR and power output after the start of the training intervention (see Figure 7.1 for details), suggesting that participants consistently kept with instructions.

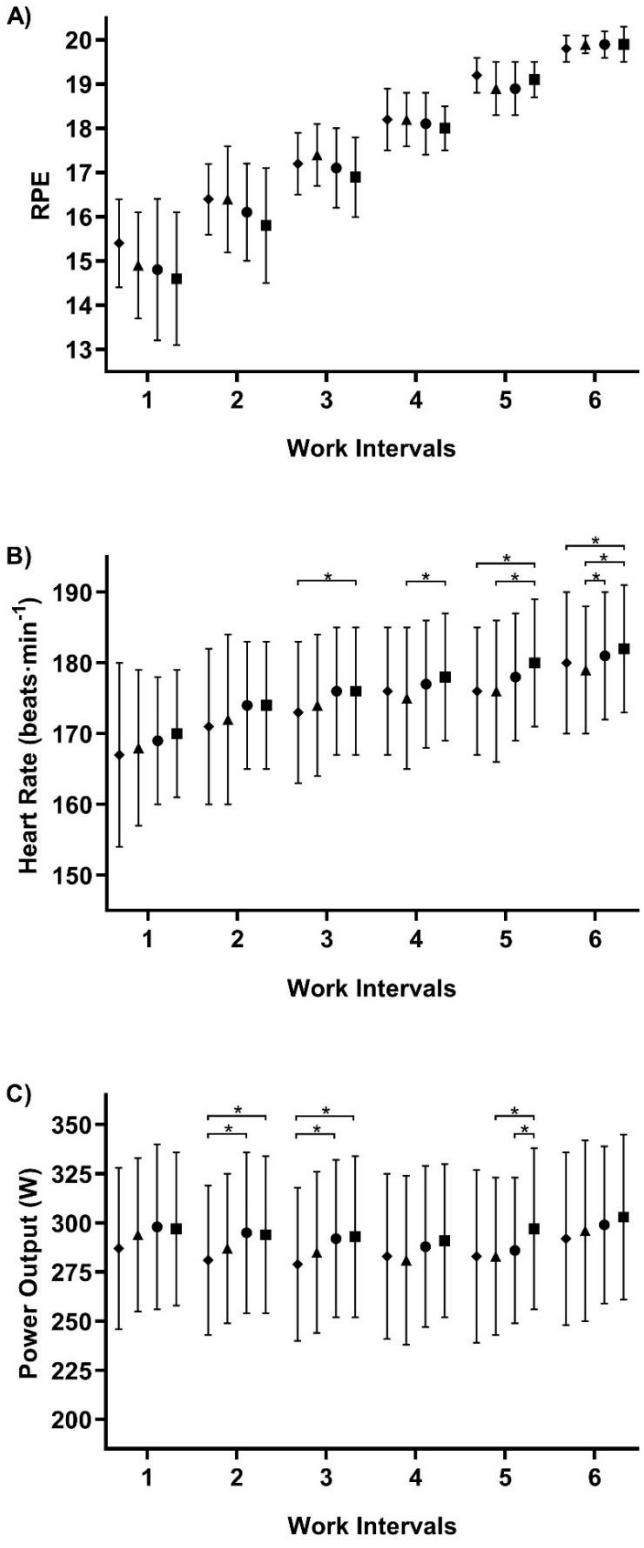

Figure 7.1 – Ratings of perceived exertion (RPE – panel A), heart rate (panel B), and power output (panel C) of each work interval of the self-paced interval training session (mean ± SD). Diamonds, triangles, circles, and squares represent weeks 0, 7, 11, and 15, respectively. * denotes significant difference (all $P \leq 0.042$).

Changes over the 16 weeks of the study were evident for all adaptive response variables, except gross efficiency (Figure 7.2), when considering all participants together. During the control phase (from week 0 to 7), $\dot{W}_{max}$ and power output associated with 4 mmol·L^{-1} [La^{-}] increased by 11 W ($P < 0.001$) and 8 W ($P = 0.027$), respectively, but there was no change for any other adaptive response (all $P \geq 0.414$). During the training intervention (from week 7 to 15), $\dot{V}O_{2max}$ increased by 0.215 L·min^{-1} ($P = 0.038$), $\dot{W}_{max}$ increased by 14 W ($P < 0.001$), and body mass increased by 1.1 kg ($P = 0.009$). While there was also an increasing trend for $\dot{W}_{max\text{-}SP}$ from week 7 to 15 (8 W, $P = 0.085$), it reached statistical significance only compared with week 0 (12 W, $P = 0.014$). Power output associated with 4 mmol·L^{-1} [La^{-}] did not increase further from week 7 ($P = 0.636$). When changes in adaptive response variables were modelled, a group difference was evident only for gross efficiency (%$\dot{W}_{max\text{-}SP}$ group: -0.8%, $P = 0.044$). However, adding a testing occasion-group interaction did not further improve the gross efficiency model ($P = 0.119$).

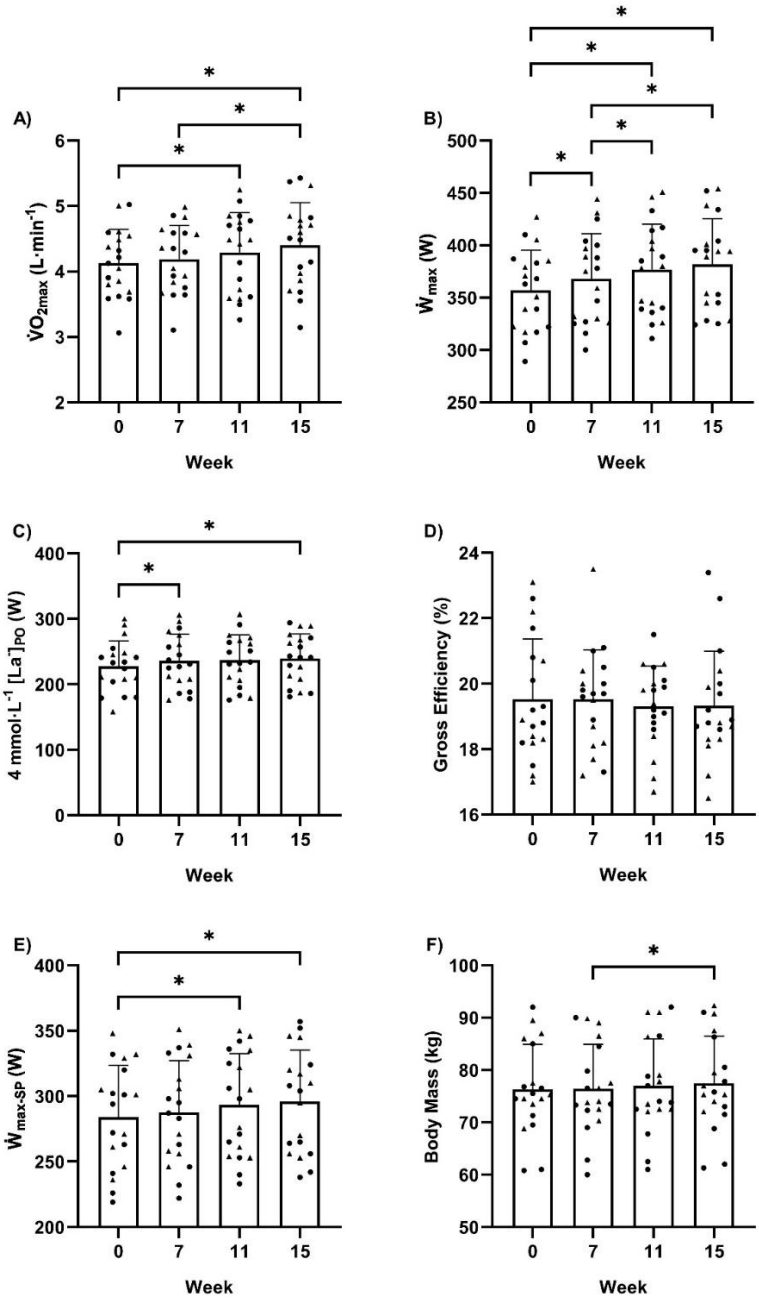

Figure 7.2 – Average of duplicate measures (mean ± SD) of maximal oxygen uptake ($\dot{V}O_{2max}$ – panel A), maximal work rate in an incremental test ($\dot{W}_{max}$ – panel B), power output associated with 4 mmol·L^{-1} blood lactate concentration (4 mmol·L^{-1} [La^{-}]$_{PO}$ – panel C), gross efficiency (panel D), maximal sustainable work rate in a self-paced interval training session ($\dot{W}_{max-SP}$ – panel E), and body mass (panel F). Circles represent individuals of the group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test. Triangles represent individuals of the group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session. * denotes significant difference (all $P \leq 0.044$).

After accounting for intra-individual variability associated with control and intervention phases (see Table 7.7 for fixed effects), evidence of inter-individual variability in adaptive responses was found for $\dot{V}O_{2max}$ (P = 0.003 – Table 7.8) and $\dot{W}_{max\text{-}SP}$ (P = 0.001 – Table 7.9). However, as reflected by the SD of intervention-week coefficients, there was no evidence of between-group differences in the magnitude of inter-individual variability for either variable, given that confidence intervals overlapped substantially ($\dot{V}O_{2max}$: 0.017 – 0.045 $L \cdot min^{-1} \cdot week^{-1}$ for $\%\dot{W}_{max}$ group, and 0.014 – 0.040 $L \cdot min^{-1} \cdot week^{-1}$ for $\%\dot{W}_{max\text{-}SP}$ group; $\dot{W}_{max\text{-}SP}$: 0.948 – 2.517 $W \cdot week^{-1}$ for $\%\dot{W}_{max}$ group, and 0.762 – 2.161 $W \cdot week^{-1}$ for $\%\dot{W}_{max\text{-}SP}$ group). Adding an intervention week-group interaction as a fixed factor did not improve either model (both $P \geq 0.197$). Unlike for $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$, no evidence of inter-individual variability in adaptive responses was found for $\dot{W}_{max}$ (P = 0.207), power output associated with 4 $mmol \cdot L^{-1}$ [La^{-}] (P = 0.466), gross efficiency (P = 0.348), or body mass (P = 0.173).

Table 7.7 – Fixed effects upon adaptive responses to training.

	$\dot{V}O_{2max}$ ($L \cdot min^{-1}$)	$\dot{W}_{max}$ (W)	4 $mmol \cdot L^{-1}_{PO}$ (W)	GE (%)	$\dot{W}_{max\text{-}SP}$ (W)	Body Mass (kg)
Intercept	4.127	357	227	19.5	284	76.3
Control Week	0.009	1.683	1.171	-0.004	0.578	0.015
Intervention Week	0.018	0.028	-0.688	-0.023	0.442	0.117

Formula: dependent variable = intercept + control week coefficient · x + intervention week coefficient · x. For control week, x = 0 to 15; for intervention week, x = 0 to 8 (where intervention week 1 corresponds to control week 8). $\dot{V}O_{2max}$, maximal oxygen uptake; $\dot{W}_{max}$, maximal work rate in an incremental test; 4 $mmol \cdot L^{-1}_{PO}$, power output associated with 4 $mmol \cdot L^{-1}$ blood lactate concentration; GE, gross efficiency; $\dot{W}_{max\text{-}SP}$, maximal sustainable work rate in a self-paced interval training session.

Table 7.8 – Linear mixed model estimates for maximal oxygen uptake ($L \cdot min^{-1}$).

Random Effect	Intercept	Intervention Week	Residual
SD	0.502	0.027	0.139

		Model Coefficients			Model Predictions							
					Control				Intervention		Gain	
Participant	Group	Intercept	Control Week	Intervention Week	Week 0	Week 7	Week 11	Week 15	Week 11	Week 15	Week 11	Week 15
1		3.765	0.009	0.020	3.765	3.826	3.861	3.896	3.940	4.054	0.079	0.158
3		4.312	0.009	0.045	4.312	4.373	4.408	4.443	4.589	4.805	0.181	0.361
5		3.551	0.009	-0.005	3.551	3.612	3.647	3.682	3.629	3.645	-0.018	-0.037
7		4.869	0.009	0.042	4.869	4.930	4.965	5.000	5.132	5.333	0.166	0.333
9		4.406	0.009	0.012	4.406	4.467	4.502	4.537	4.550	4.633	0.048	0.096
11	$\%\dot{W}_{max}$	3.574	0.009	-0.012	3.574	3.636	3.670	3.705	3.624	3.613	-0.046	-0.092
13		3.118	0.009	-0.009	3.118	3.179	3.214	3.249	3.177	3.175	-0.037	-0.074
15		3.854	0.009	0.015	3.854	3.915	3.950	3.985	4.010	4.106	0.060	0.121
17		4.606	0.009	0.062	4.606	4.667	4.702	4.737	4.949	5.230	0.246	0.493
19		4.271	0.009	0.024	4.271	4.332	4.367	4.402	4.463	4.594	0.096	0.192
Mean		4.033		0.019					4.206	4.319	0.078	0.155
SD		0.546		0.024					0.631	0.718	0.098	0.196
2		4.106	0.009	0.045	4.106	4.168	4.203	4.237	4.381	4.594	0.178	0.356
4	$\%\dot{W}_{max\text{-}SP}$	4.556	0.009	0.027	4.556	4.617	4.652	4.687	4.762	4.906	0.110	0.219
6		3.672	0.009	0.006	3.672	3.733	3.768	3.803	3.794	3.855	0.026	0.052

8		3.792	0.009	-0.007	3.792	3.853	3.888	3.923	3.861	3.869	-0.027	-0.053
10		4.550	0.009	-0.001	4.550	4.611	4.646	4.681	4.644	4.676	-0.002	-0.005
12		4.475	0.009	0.019	4.475	4.536	4.571	4.606	4.645	4.754	0.074	0.148
14		3.667	0.009	-0.011	3.667	3.728	3.763	3.798	3.721	3.714	-0.042	-0.085
16		4.380	0.009	0.030	4.380	4.441	4.476	4.511	4.597	4.753	0.121	0.243
18		4.886	0.009	0.042	4.886	4.947	4.982	5.017	5.150	5.353	0.168	0.336
	Mean	4.231		0.017					4.395	4.497	0.067	0.135
	SD	0.441		0.021					0.496	0.558	0.083	0.165

Formula: maximal oxygen uptake = intercept + control week coefficient · x + intervention week coefficient · x. For control week, x = 0 to 15; for intervention week, x = 0 to 8 (where intervention week 1 corresponds to control week 8). $\%\dot{W}_{max}$, group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test; $\%\dot{W}_{max\text{-}SP}$, group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session.

Table 7.9 – Linear mixed model estimates for the maximal sustainable work rate in a 6 × 4 min self-paced interval training session (W).

Random Effect	Intercept	Intervention Week	Residual
SD	39	1.451	5.440

		Model Coefficients			Model Predictions							
					Control				Intervention		Gain	
Participant	Group	Intercept	Control Week	Intervention Week	Week 0	Week 7	Week 11	Week 15	Week 11	Week 15	Week 11	Week 15
1	$\%\dot{W}_{max}$	272	0.578	-1.915	272	276	278	281	271	265	-8	-15
3		298	0.578	2.369	298	302	305	307	314	326	9	19
5		240	0.578	-0.723	240	244	246	249	243	243	-3	-6
7		332	0.578	1.521	332	336	339	341	345	353	6	12
9		292	0.578	0.389	292	296	298	300	299	303	2	3
11		262	0.578	-0.227	262	266	268	270	267	268	-1	-2
13		220	0.578	1.190	220	224	226	229	231	238	5	10
15		231	0.578	2.205	231	235	237	239	246	257	9	18
17		325	0.578	1.814	325	329	331	333	338	348	7	15
19		297	0.578	0.406	297	301	303	305	305	309	2	3
Mean		277		0.703					286	291	3	6
SD		39		1.379					40	42	6	11
2	$\%\dot{W}_{max-SP}$	329	0.578	-1.733	329	333	335	338	328	324	-7	-14
4		346	0.578	-0.926	346	350	353	355	349	347	-4	-7

6		240	0.578	0.964	240	244	247	249	251	257	4	8
8		260	0.578	-0.020	260	264	266	269	266	268	0	0
10		308	0.578	0.628	308	312	315	317	317	322	3	5
12		301	0.578	0.044	301	305	307	309	307	310	0	0
14		249	0.578	-0.415	249	253	256	258	254	255	-2	-3
16		265	0.578	2.132	265	269	271	273	280	290	9	17
18		333	0.578	0.694	333	337	339	342	342	347	3	6
	Mean	292		0.152					299	302	1	1
	SD	40		1.128					38	36	5	9

Formula: maximal sustainable work rate = intercept + control week coefficient · x + intervention week coefficient · x. For control week, x = 0 to 15; for intervention week, x = 0 to 8 (where intervention week 1 corresponds to control week 8). $\%\dot{W}_{max}$, group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test; $\%\dot{W}_{max\text{-}SP}$, group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session.

Both $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$ models yielded large residual errors relative to the variability in intervention-week slopes (Tables 7.8 and 7.9), resulting in wide confidence intervals for individual responses (Figure 7.3 – panels A and B), and making it difficult to categorise most participants. There were three and two responders for $\dot{V}O_{2max}$ in the $\%\dot{W}_{max}$ and $\%\dot{W}_{max\text{-}SP}$ groups, respectively, with the remaining participants being categorised as non-responders. There were three responders, six non-responders, and one adverse responder for $\dot{W}_{max\text{-}SP}$ in the $\%\dot{W}_{max}$ group; and one responder, seven non-responders, and one adverse responder in the $\%\dot{W}_{max\text{-}SP}$ group. However, modelled $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$ responses were not correlated (Figure 7.3 – panel C).

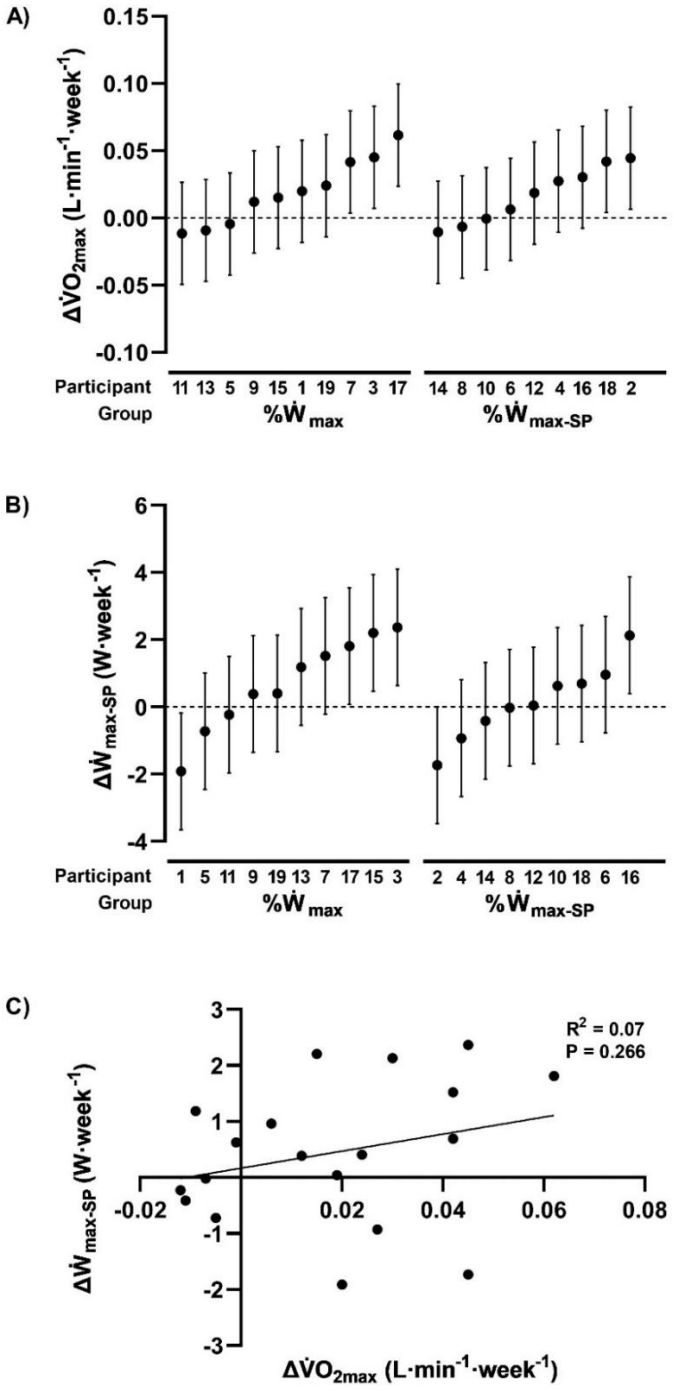

Figure 7.3 – Individual estimates with confidence intervals for weekly changes in maximal oxygen uptake ($\Delta\dot{V}O_{2max}$ – panel A) and the maximal sustainable work rate in a self-paced interval training session ($\Delta\dot{W}_{max\text{-}SP}$ – panel B) beyond the increase associated with the control phase, and relationship between both variables (panel C). $\%\dot{W}_{max}$, group in which training intensity was prescribed relative to the maximal work rate achieved in an incremental test; $\%\dot{W}_{max\text{-}SP}$, group in which training intensity was prescribed relative to the maximal sustainable work rate in a self-paced interval training session

7.4 – Discussion

In this study, we investigated acute and chronic (i.e. adaptive) responses to a training programme in which recreationally trained cyclists were split into two groups differing in exercise intensity normalisation methods, but with identical prescriptions otherwise. The findings are severalfold: a) performance in a maximal self-paced HIIT session (i.e. $\dot{W}_{max\text{-}SP}$) may be used to normalise the exercise intensity of HIIT performed at predefined work rates, particularly if premature exhaustion is to be avoided; b) RPEs and HRs elicited during HIIT may not be sensitive enough to quantify inter-individual variability in acute exercise responses; c) after accounting for sources of intra-individual variability, there was evidence of adaptive response heterogeneity for $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$ only, with no between-group differences in magnitude; d) average adaptive responses were not different between groups, meaning that the higher prevalence of incomplete training sessions in the $\%\dot{W}_{max}$ group, due to premature exhaustion, did not compromise its participants' training effect; e) uncertainty around individual adaptive responses is such that most participants were categorised as non-responders for either $\dot{V}O_{2max}$ or $\dot{W}_{max\text{-}SP}$, suggesting a limited applicability of the responder counting approach; and f) modelled changes in $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$ were not correlated. These are all novel findings with important implications that will be discussed hereafter.

7.4.1 – Acute responses to training

Since the late 1970's, several studies have been conducted in search of the best methods to normalise exercise intensity between individuals (Astorino et al., 2018, Ferguson et al., 2013, Iannetta et al., 2020, Katch et al., 1978, Lansley et al., 2011, Marini et al., 2021, McLellan and Skinner, 1981, McLellan and Skinner, 1985, Nicolò et al., 2014, Preobrazenski et al., 2019, Scharhag-Rosenberger et al., 2010, Weatherwax et al., 2019). Katch et al. (1978) and McLellan and Skinner (1985) were probably among the first to challenge the efficacy of $\%HR_{max}$ and $\%\dot{V}O_{2max}$, respectively, as the most common approaches. There is now a range of studies which highlight problems with the $\%\dot{W}_{max}$, $\dot{V}O_{2max/reserve}$, and $HR_{max/reserve}$ methods (Iannetta et al., 2020, Jamnick et al., 2020, Katch et al., 1978, Lansley et al., 2011, Mann et al., 2013, Marini et al., 2021, McLellan and Skinner, 1985, Rossiter, 2011, Scharhag-Rosenberger et al., 2010, Vollaard et al., 2009). Yet, all these methods continue to be used (Bonafiglia et al., 2019b, Bouchard et al., 1999, Bouchard et al., 2011, Coakley and Passfield, 2018b, Del Giudice et al., 2020, Hecksteden et al., 2018b, Montero and Lundby, 2017, Vollaard et al., 2009), most likely because there has been limited evidence to substantiate alternative concepts of intensity normalisation, such as %Δ, in

which maximal and submaximal anchors are considered (Lansley et al., 2011, McLellan and Skinner, 1985), CP model (Ferguson et al., 2013, Jones and Vanhatalo, 2017), and maximal self-paced intervals (Brosnan et al., 2000, Nicolò et al., 2014, Seiler and Sylta, 2017, Villerius et al., 2008). Accordingly, the present investigation demonstrated that prescribing exercise intensity of HIIT as 100%$\dot{W}_{max\text{-}SP}$ minimised performance variability between individuals compared with 80%$\dot{W}_{max}$. Only occasionally (8.3% of the sessions), did participants of the %$\dot{W}_{max\text{-}SP}$ group experience premature exhaustion throughout the training intervention, with a median completion rate of 100%. In contrast, premature exhaustion was very common (44.2% of the sessions) among participants of the %$\dot{W}_{max}$ group, with a median completion rate of 88.8% (see Table 7.4 for individual data). This was despite a similar exercise intensity between groups on average (see Table 7.3). These data thus reinforce previous studies challenging the use of %$\dot{W}_{max}$ (Iannetta et al., 2020, Jamnick et al., 2020), and provide evidence that 100%$\dot{W}_{max\text{-}SP}$ is preferable to normalise the intensity of HIIT.

The relationship between work rate and time for which it can be sustained is unique to each individual, in particular for intermittent exercise (Ferguson et al., 2013, Jones and Vanhatalo, 2017). Accordingly, it makes sense to establish a common duration, and allow individuals to select the maximal sustainable work rate, instead of presuming that a single variable can predict their exercise capacity. Prescribing exercise at 100%$\dot{W}_{max\text{-}SP}$ nevertheless assumes that a) individuals are able to pace maximal efforts to deliver performances consistent with their capacity; and b) self- and ergometer-paced performances are equivalent when the mean work rate is the same, which may not be universally true (Black et al., 2015, Thomas et al., 2013). Crucially, the present data ease concerns about both assumptions. In line with other studies (Brosnan et al., 2000, Nicolò et al., 2014, Seiler and Sylta, 2017, Villerius et al., 2008), RPE increased quasi-linearly during the self-paced HIIT sessions, approaching the ceiling in the last work interval (see Figure 7.1). Moreover, no differences between testing occasions were detected for the RPEs associated with each work interval, despite an increased HR and performance after the start of the training intervention. These observations suggest that performance gains most likely reflected an improved exercise capacity rather than a different approach to executing the task. As for the self- versus ergometer-paced performances, only participant 2 consistently struggled to complete training sessions at predefined work rates, with an 89.9% overall completion rate.

While it is tempting to conclude that maximal self-paced intervals should be adopted as a training mode, replacing intervals at predefined work rates (see Rønnestad et al. (2020), Seiler et al. (2013), and Seiler and Sylta (2017)), there are potential caveats that must be considered. Some physiological responses, such as $\dot{V}O_2$, are sensitive to large power output variations within (as demonstrated in Chapter 6) and between work intervals (Ferguson et al., 2013). Whether inter-individual variability in power output distribution would contribute to increased variability in physiological responses to HIIT is currently unknown. Therefore, if the aim is to minimise inter-individual variability, it is recommended that maximal self-paced intervals are used only to determine $\%\dot{W}_{max\text{-}SP}$.

Even though a lower performance variability between individuals was detected for the $\%\dot{W}_{max\text{-}SP}$ compared with the $\%\dot{W}_{max}$ group, RPE and HR data only partially corroborate this finding. Within the $\%\dot{W}_{max\text{-}SP}$ group, the magnitude of intra-, but not inter-individual variability, was lower for both RPE and HR (see Table 7.6). From an intra-individual perspective, this outcome is likely associated with the fact that most participants of the $\%\dot{W}_{max\text{-}SP}$ group consistently completed their training sessions, stopping at the same timepoint, whereas premature exhaustion occurred at different timepoints when participants of the $\%\dot{W}_{max}$ group struggled. This is expected, due to normal day-to-day performance variability (Midgley et al., 2007) plus the combined effects of gradual training adaptation and work rate adjustment at week 11 (see RPE in Table 7.5 for evidence of the latter effects). From an inter-individual perspective, these findings raise the possibility that RPEs and HRs elicited during HIIT are not as sensitive as performance to quantify variability and inform the normalisation of exercise intensity. Alternatively, it is conceivable that an effective normalisation of exercise intensity based upon performance does not guarantee similar physiological and perceptual responses between individuals. While more studies are required to shed light on these hypotheses, it is important to underscore that RPE and HR data were modelled to factor in the fixed effects of group, training session, and work interval, meaning that the present estimates are conservative compared with other studies (Katch et al., 1978, Lansley et al., 2011, Scharhag-Rosenberger et al., 2010, Vollaard et al., 2009), and certainly closer to the true inter-individual variability (Hecksteden et al., 2018b, Voisin et al., 2019). Unless the pitfalls inherent to the analysis of raw variability are avoided (Atkinson et al., 2019, Hecksteden et al., 2018b, Voisin et al., 2019, Williamson et al., 2017), it is unlikely that future investigations will aid the interpretation of these results.

7.4.2 – Chronic responses to training

Since the influential work of Bouchard et al. (1999) investigating the heritability of $\dot{V}O_{2max}$ responses to training, several studies have been published in which authors claimed that the extent to which each individual adapts to a standardised programme is fairly unique (Astorino et al., 2018, Bonafiglia et al., 2019b, Coakley and Passfield, 2018b, Del Giudice et al., 2020, Hecksteden et al., 2018b, Montero and Lundby, 2017, Preobrazenski et al., 2019, Vollaard et al., 2009, Weatherwax et al., 2019). However, apart from Hecksteden et al. (2018b), these studies did not account for all sources of variability affecting the observed inter-individual variability (Atkinson et al., 2019, Hecksteden et al., 2018b, Voisin et al., 2019, Williamson et al., 2017), prompting questions as to the existence of true adaptive response heterogeneity (Williamson et al., 2017). By following the best design and analytical practices (Hecksteden et al., 2018b, Voisin et al., 2019), the current study demonstrates that variability between individuals in $\dot{W}_{max}$, power output associated with 4 $mmol \cdot L^{-1}$ [La^{-}], gross efficiency, and body mass responses to a HIIT programme are likely a manifestation of intra-individual variability associated with the control phase and/or the intervention phase itself. Importantly, this interpretation is strengthened by the fact that duplicate measures were averaged to minimise day-to-day biological and technical variability, making it easier to identify a true inter-individual variability (if present) (Voisin et al., 2019). Adaptive response heterogeneity was nevertheless detected for $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$, even though the latter variable was not analysed in duplicates. Together, these distinct outcomes indicate that inter-individual variability in training adaptations can occur, although it may be difficult to demonstrate statistically when all confounding sources of variability are accounted for and/or the magnitude of changes associated with an intervention is relatively small.

Upon re-analysis of the HERITAGE family study data (Bouchard et al., 1999), Shephard et al. (2004) has demonstrated that the true inter-individual variability in $\dot{V}O_{2max}$ adaptive responses was much smaller than originally estimated. The raw SD of 0.010 $L \cdot min^{-1} \cdot week^{-1}$ represented in reality 0.007 or 0.006 $L \cdot min^{-1} \cdot week^{-1}$, whether a two-day or a two-week test-retest CV for $\dot{V}O_{2max}$ was considered, respectively, to factor in the intra-individual variability expected for assessments conducted 20 weeks apart. Given that Shephard et al. (2004) were not able to account for intra-individual variability associated with identical training programmes, either through repeated testing or repeated interventions (Hecksteden et al., 2018b, Voisin et al., 2019), it is likely that the 0.007-0.006 $L \cdot min^{-1} \cdot week^{-1}$ figure still overestimated the true inter-individual variability. Accordingly, the question that arises is

whether recreationally trained cyclists, as employed herein, are more susceptible to adaptive response heterogeneity than sedentary individuals, as employed in the HERITAGE family study (Bouchard et al., 1999) and elsewhere (Hecksteden et al., 2018b). The inter-individual variability in $\dot{V}O_{2max}$ responses reached an SD of 0.027 $L \cdot min^{-1} \cdot week^{-1}$ in the current study, a much larger figure than those estimated by Shephard et al. (2004) (see above), and Hecksteden et al. (2018b) as 0.042 $ml \cdot kg^{-1} \cdot min^{-1} \cdot week^{-1}$. In theory, all sedentary individuals are far from reaching their genetic potential for $\dot{V}O_{2max}$ improvements, whereas this might not be the case with recreationally trained cyclists, resulting in inconsistent adaptive gains between individuals of the latter cohort. Further studies are necessary to test this hypothesis.

Interestingly, evidence of adaptive response heterogeneity for $\dot{W}_{max\text{-}SP}$ was also found, implying that the extent to which participants improved intermittent exercise performance varied (with an SD of 1.451 $W \cdot week^{-1}$). While no other studies were identified to compare this result with, it suggests that $\dot{W}_{max\text{-}SP}$ is characterised by a high signal-to-noise ratio, being sensitive to small changes in exercise capacity, and thus suitable as an intensity prescription benchmark. On the contrary, adaptive response heterogeneity was not detected for $\dot{W}_{max}$. These findings are consistent with the fact that 100%$\dot{W}_{max\text{-}SP}$ successfully normalised the completion rates of HIIT, while 80%$\dot{W}_{max}$ often led to premature exhaustion (see "acute responses to training" above).

Despite the evidence in favour of $\dot{W}_{max\text{-}SP}$ as a benchmark for HIIT prescription, there were no between-group differences in the magnitude of adaptive variability, either for $\dot{V}O_{2max}$ or $\dot{W}_{max\text{-}SP}$. In contrast to the study hypothesis, it may be that adaptive responses at the individual level are too complex to always reflect the manipulation of a single element of training prescription (i.e. how exercise intensity is normalised). Mann et al. (2014) have listed factors unrelated to the training intervention that are known to affect adaptive responses, including genetics, nutrition, and recovery (i.e. from one training session to another). While genetics is believed to account for approximately 50% of the inter-individual variability in $\dot{V}O_{2max}$ responses to a training programme (Bouchard et al., 1999, Bouchard et al., 2011), the extent to which training prescription, nutrition, and recovery exert their influence, in isolation or combined, is unknown. Given that the average changes in $\dot{V}O_{2max}$, $\dot{W}_{max}$, power output associated with 4 $mmol \cdot L^{-1}$ [La^{-}], gross efficiency, $\dot{W}_{max\text{-}SP}$, and body mass were also not different between groups, it may be speculated that fine-tuning the

prescription of exercise intensity is irrelevant from an adaptive point of view. To shed light on this possibility, it is useful to analyse how the current results fit with the literature.

McLellan and Skinner (1981) compared the inter-individual variability in $\dot{V}O_{2max}$ responses between groups; one in which exercise intensity was normalised as $\%\dot{V}O_{2max}$, and another in which exercise intensity was normalised as %GET. No between-group differences were detected for the magnitude of inter-individual variability. Likewise, the dataset of Preobrazenski et al. (2019), which included $\dot{V}O_{2max}$, $\dot{W}_{max}$, and power output associated with 4 $mmol \cdot L^{-1}$ [La^{-}], reveals a similar magnitude of inter-individual variability between groups differing in how exercise intensity was normalised (i.e. $65\%\dot{W}_{max}$ versus first negative stage of the talk test). Current results therefore corroborate these previous findings. On the other hand, when comparing the $\%HR_{reserve}$ method with an individualized approach using the HR associated with each ventilatory threshold, Weatherwax et al. (2019) concluded that how exercise intensity is normalised affects the inter-individual variability in $\dot{V}O_{2max}$ responses. Upon detailed inspection, however, it becomes apparent that the individualized approach group trained at a higher intensity on average and made a larger $\dot{V}O_{2max}$ gain. As Weatherwax et al. (2019) relied on the responder counting approach, which has been shown to reflect the magnitude of mean differences rather than inter-individual differences (Atkinson et al., 2019) (more on this below), their inference could be questioned.

Even though the bulk of evidence indicates that adaptive response heterogeneity is not directly influenced by how exercise intensity is normalised, a small contribution cannot be discarded. Preobrazenski et al. (2019) also revealed that the mean [La^{-}] of the first training session was positively associated with $\dot{V}O_{2max}$ changes within the $\%\dot{W}_{max}$ group, while Gaskill et al. (2001c) showed that training intensity in the HERITAGE family study, originally normalised as $\%\dot{V}O_{2max}$ (Bouchard et al., 1999), accounted for 26% of the gains in the $\dot{V}O_2$ associated with GET when expressed as %GET. In other words, the higher the intensity relative to GET, the greater the GET gain is (Gaskill et al., 2001c). These two studies provide some evidence that the metabolic stress experienced by each individual is associated with their adaptive response (Mann et al., 2013, Mann et al., 2014). Thus, it may be that sample sizes of less than twenty participants per group, as employed herein and elsewhere (McLellan and Skinner, 1981, Preobrazenski et al., 2019, Weatherwax et al., 2019), are not always enough to detect a potential relationship between inter-individual variability in acute exercise responses and inter-individual variability in adaptive responses

to a training programme. This possibility requires careful consideration by those involved in the design of future studies.

One method that has been frequently adopted to investigate inter-individual variability in adaptive responses to a training programme is the responder counting approach (Astorino et al., 2018, Bonafiglia et al., 2019b, Bouchard et al., 1999, Coakley and Passfield, 2018b, Del Giudice et al., 2020, Hecksteden et al., 2018b, Montero and Lundby, 2017, Vollaard et al., 2009, Weatherwax et al., 2019). While definitions for responders, non-responders, and adverse responders vary between studies, constituting a problem in itself (see Hecksteden et al. (2018b) and Voisin et al. (2019) for an overview), it has been argued that this is a flawed approach for two main reasons: a) any observed response may simply reflect intra-individual variability of different sorts (Atkinson et al., 2019, Hecksteden et al., 2018b, Voisin et al., 2019, Williamson et al., 2017); and b) the number of responders, non-responders, and adverse responders of a sample is expected to be consistent with a normal distribution, reflecting deviations of the mean as a result of training, rather than the true magnitude of adaptive response heterogeneity (Atkinson et al., 2019). In light of these criticisms, the standard error of the participant-by-intervention week interaction was used to calculate confidence intervals associated with individual adaptive responses for $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$. As results demonstrate, most participants were classified as non-responders due to the uncertainty with which individual responses are estimated. Indeed, for both $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$ models, there was a large residual error compared with the inter-individual variability in intervention-week slopes, suggesting a great level of intra-individual variability. These findings therefore corroborate previous demonstrations that the responder counting approach may be untenable for the purposes of generalisation (Atkinson et al., 2019, Hecksteden et al., 2018b).

Another result that deserves attention is that modelled gains in $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$ resulting from the training intervention did not correlate, despite $\dot{V}O_{2max}$ being generally considered the main determinant of endurance performance (Joyner and Coyle, 2008). Björklund et al. (2007) also found no correlation between $\dot{V}O_{2max}$ and TTE during a HIIT session, whilst Daniels et al. (1978) and Vollaard et al. (2009) reported no association between $\dot{V}O_{2max}$ changes and time-trial performance changes following a training intervention. Taken together, these findings suggest that the scientific interest in inter-individual variability in

adaptive responses to training should perhaps shift from $\dot{V}O_{2max}$ to performance when it comes to athletes.

7.4.3 – Acute versus chronic studies

Most studies on exercise intensity normalisation can be categorised into three groups: a) those that demonstrated how work rate targets based on percentages of a maximal benchmark (e.g. 70%$\dot{V}O_{2max}$, 60%$\dot{W}_{max}$) vary regarding the intensity domain within which exercise would be performed (Iannetta et al., 2020, Katch et al., 1978); b) those that assessed inter-individual variability in performance, physiological, and/or perceptual responses to acute bouts of exercise (Lansley et al., 2011, McLellan and Skinner, 1985, Scharhag-Rosenberger et al., 2010, Vollaard et al., 2009); and c) those that compared inter-individual variability in training adaptations between groups differing in how exercise intensity was normalised (McLellan and Skinner, 1981, Preobrazenski et al., 2019, Weatherwax et al., 2019). The rationale linking these rather distinct experimental designs is that large inter-individual variability in acute exercise responses is likely to manifest as large inter-individual variability in adaptive responses to a training programme (Mann et al., 2014). This theory is based on molecular biology evidence that chronic adaptations to a training programme originate from the cumulative effects of transient homeostatic perturbations associated with each exercise session (Egan and Zierath, 2013, Perry et al., 2010). The findings of the present study and others (McLellan and Skinner, 1981, Preobrazenski et al., 2019) suggest that future investigations should look at acute exercise responses to different methods of exercise intensity normalisation rather than adaptive responses, thus avoiding waste of time and resources.

7.4.4 – Limitations

One relevant characteristic of this study is that the total training load was not only dependent on laboratory-based training sessions as was the case in other similar investigations (McLellan and Skinner, 1981, Preobrazenski et al., 2019, Weatherwax et al., 2019). While the experimental design (with a control phase prior to the intervention) and analytical procedures permitted that this source of variability was accounted for, it cannot be discarded the possibility that participants changed their habitual training routine after the start of the intervention, affecting the magnitude of inter-individual variability in adaptive responses. Despite the best efforts to persuade participants of the importance of documenting their

training load, very few participants did so with sufficient detail to provide insights in this respect.

7.4.5 – Conclusions

In summary, the evidence reported in this study suggests that $\dot{W}_{max\text{-}SP}$ may be used to normalise the intensity of HIIT performed at predefined work rates. This approach prevents premature exhaustion, although it does not necessarily minimise inter-individual variability in RPE and HR. The inter-individual variability in adaptive responses following a training intervention, although only detected for $\dot{V}O_{2max}$ and $\dot{W}_{max\text{-}SP}$, was similar in magnitude between groups differing only in how exercise intensity was normalised (i.e. $100\%\dot{W}_{max\text{-}SP}$ vs. $80\%\dot{W}_{max}$). Similarly, there were no between-group differences in the magnitude of average responses to training. These latter results underline the complexity of the relationship between acute training dose and chronic adaptations.

Chapter 8 – General discussion

8.1 – Contribution

In light of the inter-individual variability in training adaptations that is typically reported in many studies (Astorino and Schubert, 2014, Bouchard et al., 1999, Coakley and Passfield, 2018b, Del Giudice et al., 2020, Hecksteden et al., 2018b, Maturana et al., 2021, Vollaard et al., 2009, Weatherwax et al., 2019, Williams et al., 2019), there have been several attempts to uncover the biological underpinnings of such variability (Mann et al., 2014, Maturana et al., 2021, Meyler et al., 2021, Sarzynski et al., 2017, Skinner et al., 2001). In particular, some researchers have hypothesised that inter-individual variability in physiological adaptations may result, at least in part, from a how exercise intensity is normalised across participants of a given training intervention (Mann et al., 2014, Meyler et al., 2021, Vollaard et al., 2009, Weatherwax et al., 2019). In other words, training interventions that have typically been referred to as standardised and methodologically robust, such as the HERITAGE family study (Bouchard et al., 1995, Gagnon et al., 1996), may have failed to provide a comparable adaptive stimulus across individuals. This is because the methods that are most commonly utilised to prescribe training intensity have been shown not to pass the validity test (Jamnick et al., 2020, Mann et al., 2013, Meyler et al., 2021), as evidenced by the domain allocation of each individual's training (Iannetta et al., 2020, Weltman et al., 1990) and the large variability in physiological, metabolic, and perceptual responses to exercise between individuals (Baldwin et al., 2000, Egger et al., 2016, Gass et al., 1991, Lansley et al., 2011, Scharhag-Rosenberger et al., 2010). Accordingly, this thesis was conceived to address the methodological aspect of intensity prescription for HIIT as a possible source of adaptive variability, particularly because the normalisation of intensity for this type of training has been under-researched.

In Chapter 4, it was demonstrated that %Δ should not be used to normalise the exercise intensity of HIIT. There was large inter-individual variability in TTE, cardiorespiratory responses, [La^{-}], and RPE, suggesting that a comparable adaptive stimulus across individuals would not be achieved if training sessions were systematically repeated. A high level of intra-individual variability was also observed for most dependent variables, although to a lesser extent if compared with the magnitude of inter-individual variability. Thus, it is possible to conclude that the large inter-individual variability observed cannot be accounted for by intra-individual variability only. In Chapter 5, it was demonstrated that out of several methods commonly used for exercise intensity normalisation (i.e. %Δ, %$\dot{W}_{max}$, percentage of the average work rate sustained in a 20-min time-trial, and percentage of W' expenditure),

none actually minimised the inter-individual variability in performance, physiological, and perceptual responses to HIIT. In fact, TTE, cardiorespiratory responses, [La^-], RPE and muscle tissue oxygenation were all equally variable across conditions, no matter how exercise intensity was normalised. Thus, it was concluded that other methods should be used for the effective intensity normalisation of HIIT, with further studies being necessary to determine the optimal prescription approach. In Chapter 6, it was demonstrated that prescribing HIIT with work intervals of variable power output, rather than constant, may be an effective strategy to maximise the cardiorespiratory stress of training sessions without incurring additional effort (as quantified by RPE) or metabolic stress (as quantified by [La^-]). In Chapter 7, it was demonstrated that the maximal sustainable work rate in a self-paced HIIT session can be used to normalise the intensity of ergometer-paced training sessions of identical duration and format. In fact, most sessions were fully completed by participants training at the maximal sustainable work rate, whereas sessions performed at 80%$\dot{W}_{max}$ were often interrupted prematurely due to exhaustion. This was despite a similar training intensity between groups (on average) and similar magnitudes of inter-individual variability in training HR and RPE. It was also demonstrated in Chapter 7 that the magnitude of inter-individual variability in adaptive responses resulting from training, although only detected for $\dot{V}O_{2max}$ and self-paced HIIT performance, was similar between groups differing in how exercise intensity was normalised. There were also no between-group differences in mean training adaptations. Chapter 7 therefore demonstrates no relationship between how exercise intensity is normalised and the magnitude of inter-individual variability in adaptive responses to training. Overall, this thesis a) challenges some of the current approaches for the normalisation of exercise intensity, at least with regard to HIIT, b) provides evidence that keeping a constant power output during work intervals may not be the best to maximise the training effect, c) demonstrates that self-paced performances may be used as a benchmark for intensity prescription, and d) questions the belief that how training intensity is normalised affects the variability in adaptive responses.

The %Δ method of intensity prescription, in which both GET and $\dot{V}O_{2max}$ are considered to normalise exercise intensity, has been advocated by Lansley et al. (2011) as an effective approach to reducing the inter-individual variability in acute exercise responses. However, the results of Chapters 4 and 5 suggest this might not be the case for HIIT. In Chapter 4, the same HIIT session was repeated on four occasions, with exercise intensity prescribed as 70%Δ. This permitted that inter-individual variability could be modelled by accounting for

intra-individual variability, an approach that has been rarely implemented to investigate the normalisation of exercise intensity (see Egger et al. (2016) and Faude et al. (2017) for exceptions). Compared with raw estimates, modelled estimates tend to be smaller, as some of the observed inter-individual variability reflects different sources of intra-individual variability (Atkinson and Batterham, 2015, Egger et al., 2016, Hecksteden et al., 2018b, Shephard et al., 2004, Voisin et al., 2019). Yet, there was still a large inter-individual variability for most measures. This can be best illustrated by TTE, in which for a grand mean of 20.3 min there was an inter-individual SD of 9.3 min, representing a CV of 45.8%. In Chapter 5, HIIT sessions were each performed at slightly different work rates as four methods of intensity normalisation were tested (including 70%Δ). Accordingly, the logarithm of TTE was modelled as a function of different expressions of relative intensity. Despite the distinct modelling approach, the inter-individual CV was also high, reaching 53.7%. Importantly, expressing exercise intensity as %$\dot{V}O_{2max}$ elicited a similar CV of 50.4%. Altogether, Chapters 4 and 5 refute the notion that %Δ is inherently a better method than %$\dot{V}O_{2max}$.

If anything, the modelled CVs for TTE reported in Chapters 4 and 5 are higher than the raw estimates reported elsewhere (Coyle et al., 1988, Lansley et al., 2011, McLellan and Skinner, 1985, Scharhag-Rosenberger et al., 2010). Inter-individual CVs for TTE reached 42.8%, 43.4%, 42.5%, and 41.8% for continuous exercise performed at 75% (Scharhag-Rosenberger et al., 2010), 88% (Coyle et al., 1988), 90% (Lansley et al., 2011), and 95%$\dot{V}O_{2max}$ (McLellan and Skinner, 1985), respectively. It may therefore be speculated that performance during HIIT is more unpredictable compared with continuous exercise. While this may be true, the results of this thesis suggest this is not necessarily an obstacle to attaining an effective intensity normalisation for HIIT. In Chapter 5, it was demonstrated that HIIT prescribed as %$\dot{W}_{max}$ elicits a large inter-individual variability in TTE, with a CV of 44.2%. Unsurprisingly, when training was prescribed at 80%$\dot{W}_{max}$, as part of the study described in Chapter 7, some participants often became exhausted prematurely, being unable to complete the entire HIIT sessions. However, most sessions were completed by participants of the group training at the power output representing their maximal self-paced performance, despite the similar training intensity on average, and the equally exhaustive nature of HIIT. Thus, it is concluded that self-paced HIIT performance is the best predictor of ergometer-paced HIIT performance.

The aforementioned points of discussion are based upon the assumption that an effective normalisation of exercise intensity is best achieved when a given prescription elicits similar performance across individuals. This is a reasonable assumption, as it finds precedent in the work rate-time relationship that characterises performance (Billat et al., 1999a, Hofmann and Tschakert, 2017, Jones and Vanhatalo, 2017, Nordesjö, 1974). However, there is no evidence to suggest that maximal performances for a given duration elicit similar adaptive stimulus across individuals. In fact, it may be difficult to establish such a relationship, given that biopsy-derived molecular markers of adaptive response are generally less reliable than maximal exercise performances (see Islam et al. (2019) and Currell and Jeukendrup (2008) for comparison). Therefore, one could argue that minimising inter-individual variability in cardiorespiratory and metabolic responses to exercise, rather than performance, should be the goal if optimal intensity prescription methods are to be determined. This view can be substantiated by a large body of evidence demonstrating the existence of cardiorespiratory and metabolic stress profiles that are specific to each intensity domain (Jamnick et al., 2020, Jones et al., 2011, Rossiter, 2011). In this respect, Chapter 5 demonstrates that none of the tested methods of intensity normalisation was effective in minimising acute exercise responses to HIIT. In contrast, Chapter 7 demonstrates that performance was the only variable sensitive to the method of prescription. The magnitude of inter-individual variability in both HR and RPE was similar between groups, but not training session completion rates, suggesting that performance would theoretically be the best parameter to judge the efficacy of an intensity prescription method, at least when it comes to HIIT.

Given the results of Chapter 6, in which varied-intensity work intervals were shown to increase the cardiorespiratory demand of a HIIT session compared with constant-intensity work intervals (i.e. higher time at >90%$\dot{V}O_{2max}$, %$\dot{V}O_{2max}$ sustained, and total $\dot{V}O_2$), it may be speculated that this type of training would lead to greater $\dot{V}O_{2max}$ gains if training sessions were systematically repeated (Billat, 2001, Buchheit and Laursen, 2013, Midgley and McNaughton, 2006). While a training study would be necessary to test this hypothesis, there are also immediate implications for the methodological aspect of HIIT prescription. Particularly because varied-intensity work intervals did not affect HR, RPE, or [La^-], it may be questioned whether it is indeed important to perform HIIT at pre-defined work rates. Ultimately, this is a question of whether methods of exercise intensity normalisation are necessary if HIIT can also be prescribed as a maximal self-paced performance, in which power output is expected to vary less compared with the training protocol described in

Chapter 6. Perhaps, finding an answer to these questions is difficult for scientists, but may be very simple for coaches and athletes, given that self-paced HIIT has been referred to as how elite athletes train (Brosnan et al., 2000, Nicolò et al., 2014, Rønnestad et al., 2020, Seiler et al., 2013, Seiler and Sylta, 2017, Villerius et al., 2008).

One common theory that provides the basis for this thesis is that an effective exercise intensity normalisation contributes to minimising inter-individual variability in adaptive responses to training. However, the results of Chapter 7 raise questions about this theory, particularly because other studies were also not able to detect a cause-and-effect relationship between how exercise intensity is normalised and the magnitude of adaptive response heterogeneity (Johnson et al., 2017, McLellan and Skinner, 1981, Preobrazenski et al., 2019, Swart et al., 2009). Even though the conclusions of Weatherwax et al. (2019) and Wolpern et al. (2015) deviate from the conclusions of most authors, they failed to isolate the effect of the prescription method from the effect of the average training intensity. Taken together, the majority of evidence points to these possibilities: training adaptations are not sensitive to small changes in exercise intensity and duration, as it would be expected if methods of intensity normalisation are exchanged with one another, and/or training adaptations are so complex, representing the interaction of multiple biological and behavioural elements (Mann et al., 2014, Meyler et al., 2021, Sarzynski et al., 2017), that only large-scale studies would be able to reveal a possible connection between how exercise intensity is normalised and the magnitude of adaptive variability. Nevertheless, a cautionary approach is warranted until the evidence is totally clear. This means that researchers investigating inter-individual variability in adaptive responses to training should try to minimise all sources of bias, which may, according with the findings of this thesis, originate from how the intensity of HIIT is prescribed.

8.2 – Practical applications

It may be easier to normalise exercise intensity between individuals at intensities within the moderate and heavy compared with the very heavy intensity domain. This is because a physiological steady state is attained during exercise within the moderate and heavy domains, whereas a progressive physiological disturbance that culminates in exhaustion characterises the very heavy domain (Jamnick et al., 2020, Jones et al., 2011, Rossiter, 2011). This may explain why less work has been done to support the prescription of exhaustive exercise, and HIIT in particular (see Section 2.5 – Methods of intensity prescription),

compared with steady-state exercise. Notwithstanding this literature limitation, some possible solutions to prescribe exercise intensity within each domain are presented hereafter, based upon the findings of this thesis and the latest methodological developments.

Recently, Iannetta et al. (2019b) have proposed a practical approach for determining $\dot{V}O_2$ mean response time of ramp-incremental tests. It requires a single 6-min step transition at a constant work rate within the moderate-intensity domain, and it can be performed as part of the warm-up of a testing session. The difference between the power output associated with steady-state $\dot{V}O_2$ and the power output associated with the same $\dot{V}O_2$ during the ramp-incremental test can be converted from watts to seconds, based on the test ramp rate ($W \cdot min^{-1}$), to produce a reliable measure of the mean response time (Iannetta et al., 2019b). This simple solution provides researchers with more confidence when identifying the power output required to elicit a target $\dot{V}O_2$, and also the power output associated with the transition from moderate to heavy intensity domains (i.e. GET). In subsequent work, Iannetta et al. (2019a) have shown that, by taking into account the $\dot{V}O_2$ mean response time of a 5 $W \cdot min^{-1}$ ramp test, the transition from the heavy-to-very heavy domains can be identified as the work rate associated with RCP. Although a 5 $W \cdot min^{-1}$ ramp test may be too long for obtaining the true $\dot{V}O_{2max}$ of certain individuals (Midgley et al., 2008), to perform a shorter ramp-incremental test (e.g. 25 $W \cdot min^{-1}$), on a different day, is still much easier than undergoing multiple sessions to obtain other transition markers of the heavy-to-very heavy boundary such as CP (Maturana et al., 2018, Muniz-Pumares et al., 2019), or the maximal metabolic steady state (Beneke, 2003, Billat et al., 2003). By using Iannetta's protocols (Iannetta et al., 2019a, Iannetta et al., 2019b), and a TTE test at a work rate above $\dot{W}_{max}$ (of the short ramp-incremental test) to confirm $\dot{V}O_{2max}$ (Midgley et al., 2008, Poole and Jones, 2017), it is possible to get valid measures of GET, RCP and $\dot{V}O_{2max}$ with just two laboratory visits.

Once the power output-$\dot{V}O_2$ relationship and the boundaries of the intensity domains are established (Iannetta et al., 2019a, Iannetta et al., 2019b), %GET may be used for exercise intensity normalisation within the moderate domain, and %Δ for exercise within the heavy domain. However, there is a caveat to the use of %Δ. McLellan and Gass (1989) have shown that %Δ normalises metabolic and cardiorespiratory responses during exercise at 33%Δ, but not at 67%Δ. These data suggest that instead of GET and $\dot{V}O_{2max}$ (Lansley et al., 2011, McLellan and Gass, 1989, McLellan and Skinner, 1985), GET and RCP should be taken into

account to avoid a wide Δ, which might place individuals in different intensity domains during training.

As for the prescription of exercise within the very heavy intensity domain, a fixed power output-$\dot{V}O_2$ relationship cannot be determined based on the very nature of physiological responses to these exercise intensities (Jamnick et al., 2020, Jones et al., 2011, Rossiter, 2011). For this reason, it may be recommended to use fixed-duration time-trials (i.e. maximal-effort, self-paced exercise), or the average time-trial power output could be used for the normalisation of ergometer-paced exercise intensity (analogous to what was done for HIIT in Chapter 7). Time-trials have been successfully used to model individuals' work rate-duration relationship (Black et al., 2015, Muniz-Pumares et al., 2019), performance is usually quite reliable (Currell and Jeukendrup, 2008), and the magnitude of both RPE and f_R (i.e. strain level indicators (Nicolò et al., 2017b)) increase quasi-linearly throughout the exercise, with peak responses reached at the end (Nicolò et al., 2014, Nicolò et al., 2016). Both approaches could also be used for the prescription of HIIT as evidenced by Chapter 7 and further discussed in Section 8.1 – Contribution. When training sessions are prescribed as maximal-effort, self-paced exercise purely, there is also the advantage of allowing any given training session to be completed no matter the fatigue status or environmental conditions experienced by a given individual. However, two potential shortcomings include individuals' motivation (Wilmore, 1968) and inappropriate pacing (Aisbett et al., 2009, Mattern et al., 2001) as sources of underperformance. If not controlled for, these factors may potentially induce larger inter-individual variability in physiological responses than would be expected.

Whether these suggestions are indeed able to minimise the inter-individual variability in performance, cardiorespiratory and perceptual responses to exercise in each intensity domain needs further investigation. Nevertheless, in the study with the largest $\dot{V}O_{2max}$ gain ever reported, in which little to no inter-individual variability was detected, Hickson et al. (1977) prescribed high-intensity training with a similar approach to what is proposed here. Maximal self-paced continuous training was chosen for the running sessions, whereas the work rate for cycling-based HIIT was adjusted by researchers to allow $\dot{V}O_{2max}$ to be attained during each work interval. As participants were required to finish all work intervals, Hickson et al. (1977) presumably adjusted the work rate to yield each individual's maximal sustainable work rate for each training session, which certainly triggered physiological and metabolic

responses typical of self-paced HIIT. Despite its small sample size, the study of Hickson et al. (1977) may provide some evidence that the proposed framework of intensity prescription serves its purpose.

8.3 – Future directions

Several potential research avenues emerge from the findings of this thesis. First, more research is necessary, in general, to investigate the validity of different expressions of exercise intensity. Ideally, inter-individual variability in performance, physiological and metabolic responses to exercise should be quantified through modelling approaches that take into account intra-individual variability as implemented in Chapters 4 and 5. Except for Egger et al. (2016) and Faude et al. (2017), researchers have mostly ignored the fact that the observed inter-individual variability is "contaminated" with intra-individual variability of different sorts (Atkinson and Batterham, 2015, Egger et al., 2016, Hecksteden et al., 2018b, Shephard et al., 2004, Voisin et al., 2019). Second, training studies are necessary to confirm that varied-intensity work intervals indeed maximise the adaptive stimulus to increase $\dot{V}O_{2max}$ as indicated by the preliminary findings of Chapter 6. Third, future studies are required to clarify whether the use of self-paced continuous and intermittent exercise, to normalise the intensity of ergometer-paced training sessions, minimises the variability in cardiorespiratory and metabolic responses compared with more traditional prescription methods; given that only HR and RPE were assessed in Chapter 7. Fourth, researchers should compare the acute and adaptive responses elicited by self-paced and ergometer-paced training when the average training intensity is the same. Fifth, and lastly, large-scale studies are necessary to test the premise that how exercise intensity is normalised affects the magnitude of inter-individual variability in adaptive responses. As with cross-sectional studies, research design and model fitting considerations must be well planned to minimise the influence of intra-individual variability upon the estimates of inter-individual variability (Atkinson and Batterham, 2015, Egger et al., 2016, Hecksteden et al., 2018b, Shephard et al., 2004, Voisin et al., 2019).

8.4 – Conclusions

The experimental studies of this thesis demonstrate that commonly used methods of exercise intensity normalisation are not effective for the prescription of HIIT. Performance, cardiorespiratory, $[La^{-}]$, RPE, and muscle tissue oxygenation responses to HIIT varied substantially between individuals no matter how intensity was expressed. In contrast, the

maximal sustainable work rate in a self-paced HIIT session can be used to normalise the intensity of ergometer-paced training sessions of identical duration and format. However, an effective intensity normalisation on the basis of performance does not guarantee that training will produce homogeneous adaptative responses across individuals.

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