

Oxygen Uptake Kinetics: An Underappreciated Determinant of Exercise Performance

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The rate at which VO_2 adjusts to the new energy demand following the onset of exercise strongly influences the magnitude of the " O_2 deficit" incurred and thus the extent to which muscle and systemic homeostasis is perturbed. Moreover, during continuous high-intensity exercise, there is a progressive loss of muscle contractile efficiency, which is reflected in a "slow component" increase in VO_2 . The factors that dictate the characteristics of these fast and slow phases of the dynamic response of VO_2 following a step change in energy turnover remain obscure. However, it is clear that these features of the VO_2 kinetics have the potential to influence the rate of muscle fatigue development and, therefore, to affect sports performance. This commentary outlines the present state of knowledge on the characteristics of, and mechanistic bases to, the VO_2 response to exercise of different intensities. Several interventions have been reported to speed the early VO_2 kinetics and/or reduce the magnitude of the subsequent VO_2 slow component, and the possibility that these might enhance exercise performance is discussed.

The purpose of this invited commentary is to provide a brief overview of the importance of the rate at which oxygen uptake (VO_2) increases following the onset of exercise (the " VO_2 kinetics"). The dynamic features of the VO_2 response to exercise dictate the relative contribution of oxidative and nonoxidative metabolism to energy supply during exercise. We argue that the VO_2 kinetics—along with the $\text{VO}_{2\text{max}}$, exercise economy, lactate threshold, and critical power/velocity—is an important parameter of aerobic function that impacts critically on human exercise capacity.¹ Since the amount of work that can be done "anaerobically" is limited, it holds that interventions that can enhance VO_2 kinetics will increase the contribution of oxidative metabolism to energy turnover and have the potential to enhance performance.²

Oxygen Uptake Kinetics

After the starter's pistol fires to signal the beginning of a foot race, an athlete will accelerate from a stationary position to the required race pace within a few seconds. Depending on the distance (and duration) of the race and the training status

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of the athlete, the ATP turnover rate in the contracting muscle cells might increase as much as 100-fold over these first few seconds. To prevent a catastrophic reduction in muscle [ATP] (the brackets denote concentration) and almost-immediate exhaustion, ATP is resynthesized through an acceleration of both the creatine kinase reaction, with a consequent reduction in muscle [phosphocreatine], and the glycolytic rate, resulting in increased H^+ and lactate production. Simultaneously, changes in the muscle phosphorylation potential (eg, reduced ATP, increased ADP and P_i) are communicated to the mitochondria, stimulating an increased rate of oxidative phosphorylation (and hence VO_2). The "drive" to the latter depends upon the difference between the instantaneous VO_2 and the "required" VO_2 , assuming that the actual "steady-state" ATP turnover rate can be precisely matched by the ATP supply through oxidative metabolism (this assumption will not hold, of course, during exercise where the "steady-state" VO_2 requirement exceeds the individual's VO_{2max}). The necessary consequence of this is the characteristic exponential increase in VO_2 from the preexercise baseline to (or toward) the required steady-state VO_2 .³

The magnitude of the " O_2 deficit," and thus the extent of the contribution from substrate-level phosphorylation and the attendant perturbations to muscle homeostasis, is a function of the amplitude of the VO_2 response (VO_2 at steady state minus VO_2 just before the start of exercise) and the VO_2 "time constant" (a parameter that describes the rate at which VO_2 rises toward the steady state).³ For the same VO_2 amplitude, a shorter time constant (eg, 20 s, leading to the attainment of a steady state within 80 s; ie, 4 \times the time constant) will result in a 50% smaller O_2 deficit than will a longer time constant (eg, 40 s, leading to a steady state in 160 s; Figure 1A). While oxidative phosphorylation is widely agreed to be principally under "feedback" control and related ultimately to the rate of ATP hydrolysis, the extent to which VO_2 kinetics might be additionally constrained by muscle O_2 supply or by the activation of rate-limiting mitochondrial enzymes remains a source of debate.⁴ Muscle O_2 delivery does not appear to limit VO_2 kinetics in young healthy subjects but might be at least in part responsible for the slower VO_2 kinetics observed in sedentary, senescent, and diseased populations.⁴ Regardless, it is clear that faster VO_2 kinetics will spare the finite "anaerobic capacity" by reducing the fall of muscle PCr and the utilization of muscle glycogen reserves and limit the accumulation of metabolites that have been associated with the fatigue process (eg, H^+ , ADP, and P_i).²

It is important to stress that the contour of the VO_2 response to exercise differs according to the intensity "domain" within which the exercise is performed.²⁻⁵ For example, as described above, the response is essentially mono-exponential during so-called moderate-intensity exercise completed below the lactate or pulmonary gas exchange threshold (Figure 1A). At higher intensities (approximately 60 to 100% VO_{2max}); however, the early exponential VO_2 response is supplemented by a delayed-onset "slow component" that elevates VO_2 to a value above what might be expected for the work rate. This response will delay the attainment of a steady state for "heavy" exercise performed below the critical power (Figure 1B), or render it unattainable for "severe" exercise above the critical power (Figure 1C). For still higher intensities of exercise, that is, "extreme" exercise that has a "steady-state" VO_2 requirement above the individual's VO_{2max} , the exercise duration is typically so short (less than approximately 3 min) that a VO_2 slow component is not readily observed.⁵

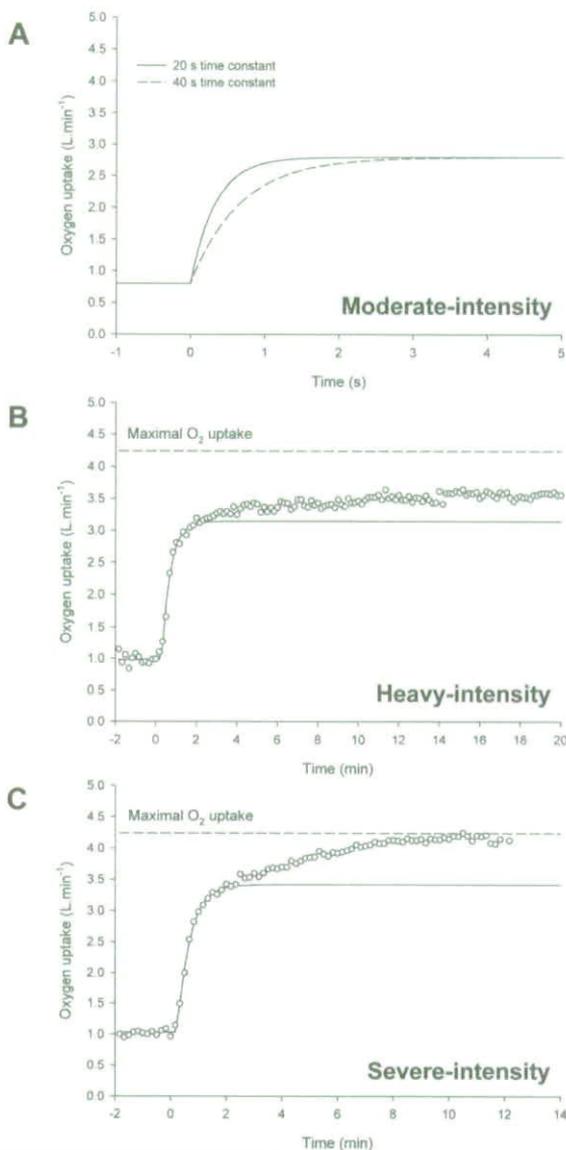


Figure 1 — Oxygen uptake responses to moderate-, heavy-, and severe-intensity exercise. Panel A: Schematic responses to moderate exercise performed at 200 W in two subjects with markedly different VO_2 kinetics. The subject with slow VO_2 kinetics (time constant = 40 s) achieves the same steady-state VO_2 as the subject with fast kinetics (time constant = 20 s) but accumulates a significantly greater O_2 deficit (slow kinetics, 1.33 L; fast kinetics 0.67 L). Panel B: The VO_2 response of a representative subject to heavy-intensity exercise (>LT, <CP), which is associated with a slow component of VO_2 kinetics that delays the attainment of a steady state. The subject was able to exercise for 20 min without duress. The solid line represents the best-fit exponential applied to the “fast” component of VO_2 , and the dashed line represents $\text{VO}_{2\text{max}}$. Panel C: The VO_2 response to severe-intensity exercise (>CP) in the same subject as panel B. Despite the power output being just 30 W higher than in panel B, the VO_2 response is distinctly different: the VO_2 rises throughout exercise, reaching $\text{VO}_{2\text{max}}$ shortly before exhaustion occurs. See text for discussion.

The VO_2 slow component is another important feature of the VO_2 kinetics that appears to be linked to the process of muscular fatigue. Essentially, the VO_2 slow component phenomenon reflects a loss of muscle efficiency; that is, maintaining the same work rate requires a progressively greater energy turnover with time, which is reflected both in a continued fall in muscle [PCr] and a continued rise in VO_2 (Figure 1B).⁶⁻⁸ When VO_2 reaches its maximum value for the exercise modality and muscle [PCr] reaches a nadir, exercise tolerance becomes severely limited (Figure 1C).^{8,9} The mechanistic basis for the VO_2 slow component remains somewhat elusive but is likely related to the activation of muscle fibers that are positioned higher in the recruitment hierarchy.¹⁰⁻¹² These "type II" fibers are generally considered to be less efficient than "type I" fibers. Given the relationship between the development of the VO_2 slow component and the process of muscle fatigue, it is clear that interventions that attenuate or eliminate the VO_2 slow component should enhance exercise performance.

Interventions to Enhance VO_2 Kinetics

Given the potential for the dynamic VO_2 response following the onset of exercise to influence the extent of the muscle metabolic perturbation and hence exercise tolerance, it is important to explore interventions which might enhance VO_2 kinetics either by speeding the early VO_2 kinetics and reducing the O_2 deficit or by reducing the magnitude of the VO_2 slow component.

Endurance exercise training is, perhaps not surprisingly, the intervention that most profoundly alters VO_2 kinetics. Cross-sectional studies show that elite endurance athletes have very fast VO_2 kinetics. For example, a VO_2 time constant of 8.5 s has been measured across the transition from standing rest to treadmill running at a speed of 16 km/h in Paula Radcliffe, the women's world marathon record holder, such that a complete steady state was achieved within about 35 s.¹³ Time constants of this order have also been reported in thoroughbred racehorses.¹³ Elite endurance athletes also have rather small VO_2 slow components during high-intensity exercise. This is, in part, due to the fact that the LT and CP occur at very high fractions of the $\text{VO}_{2\text{max}}$ in such athletes such that the "scope" for the VO_2 slow component to develop is limited.¹³

The fast VO_2 kinetics in endurance athletes raises the question of whether this is a genetic trait or a consequence of intensive training. Endurance training has been shown to result in faster initial VO_2 kinetics and a reduced VO_2 slow component.^{14,15} However, it is presently not known whether there is an "optimal" type of training session or training program that specifically "targets" the enhancement of VO_2 kinetics. Theoretically, assuming that muscle O_2 delivery is sufficient, any training intervention that increases muscle mitochondrial volume would be expected to accelerate VO_2 kinetics (Figure 2).¹⁶ In this regard, it is interesting that repeated sprint training appears to be at least as effective as low-intensity continuous endurance training in eliciting improvements in VO_2 kinetics.¹⁷ Repeated sprint training enhances muscle fractional O_2 extraction as estimated by near-infrared spectroscopy measurements,¹⁷ presumably as a consequence of increased muscle oxidative capacity.¹⁸ It should be noted that a high resting muscle [PCr] will tend to retard the rate at which VO_2 increases following the start of exercise. This is because a high muscle [PCr] will tend to blunt the arrival at the mitochondria of signals that

accelerate oxidative phosphorylation (perhaps, in particular, the free [ADP]).^{16,19} Therefore, athletes with a relatively high anaerobic capacity or distribution of type II muscle fibers, such as sprinters or middle-distance runners, will tend to have slower VO_2 kinetics than long-distance specialists even if $\text{VO}_{2\text{max}}$ values are similar.^{20,21}

An acute intervention that positively affects VO_2 kinetics is the performance of a prior bout of exercise.²² Although this type of activity has traditionally been termed *warm-up*, it is important to note that the effects of prior exercise on VO_2 kinetics are not related to changes in muscle temperature, per se.²³ It has been shown that prior exercise results in faster "overall" VO_2 kinetics, chiefly as a consequence of

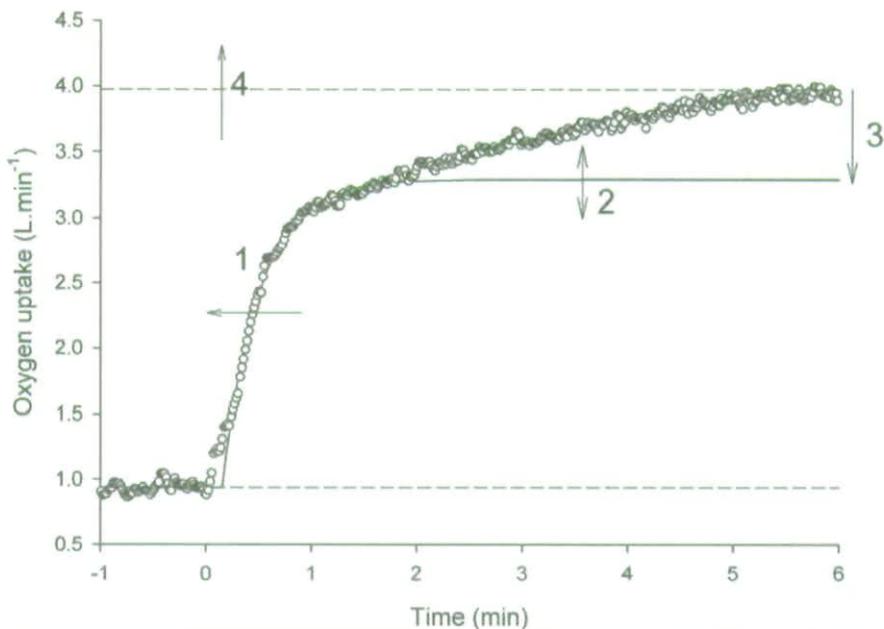


Figure 2 — Schematic of the effects on VO_2 kinetics of various interventions: (1) speeded initial (fast component) VO_2 kinetics, which serves to reduce the O_2 deficit, spare the finite "anaerobic capacity," and reduce the extent of muscle metabolic perturbation. Interventions that achieve this include interval and endurance training, and (indirectly) a fast-start pacing strategy. (2) Alteration of the VO_2 fast component amplitude, for example, as a consequence of training or the performance of prior high-intensity exercise. (3) Reduced VO_2 slow component amplitude, which reduces the O_2 cost of exercise and delays the attainment of $\text{VO}_{2\text{max}}$ during severe-intensity exercise. Endurance training, prior high-intensity exercise, hyperoxia, dichloroacetate administration, sodium bicarbonate loading, and increased dietary nitrate intake all achieve this effect, although the mechanistic basis may be different in each case. (4) Increased $\text{VO}_{2\text{max}}$, which increases the scope of the VO_2 response and thus increases the time taken for the slow component to drive VO_2 to the maximum during severe-intensity exercise. Interventions that increase bulk O_2 delivery (such as training and erythropoietin administration) will achieve this effect. In these cases, exercise tolerance can be enhanced despite an *increase* in the amplitude of the slow component. Thus, during severe-intensity exercise, both the *rate* of increase and the amplitude of the VO_2 slow component might impact on exercise performance. Solid line, best-fit of the primary VO_2 response; dashed line, $\text{VO}_{2\text{max}}$.

a reduction in the VO_2 slow component amplitude (Figure 2).^{22,23} Several studies have now shown that these changes in VO_2 kinetics with prior exercise have the potential to enhance exercise performance during the "criterion" exercise bout, but the precise combination of prior exercise intensity and the duration of the intervening recovery period that optimizes the effect remain uncertain.^{24,25} It is important that the prior exercise bout is sufficiently intense to elevate blood [lactate] if VO_2 kinetics during subsequent exercise is to be altered.²² However, it would also seem important that the initial bout is neither too intense nor the recovery interval too short to ensure that the athlete does not commence competition with, for example, depleted muscle [PCr]. The mechanistic basis for the changes in VO_2 kinetics observed following prior high-intensity exercise are probably related to an interaction between increased muscle O_2 availability, increased muscle oxidative enzyme activation, and altered motor unit recruitment patterns.²²

The pacing strategy employed by an athlete during competition might also have an impact on VO_2 kinetics and thus the performance outcome. For example, it was recently reported that, compared with an even-pace and slow-start strategy, a fast-start strategy resulted in faster VO_2 kinetics and an extended time to exhaustion during extreme exercise.²⁶ Presumably, the stimulus to accelerate VO_2 kinetics was greatest in the fast-start condition. Nevertheless, it is important to husband one's resources according to the prevailing competitive conditions and such a strategy might not be recommended in all circumstances. Pacing strategy must consider the appropriate allocation of the athlete's finite work capacity for exercise above the critical power/velocity: ideally, this should be exhausted at the exact moment the athlete crosses the finishing line.²⁷

Several nutritional interventions have the potential to affect VO_2 kinetics. The drug dichloroacetate, which activates the pyruvate dehydrogenase enzyme complex allowing greater supply of acetyl groups to the mitochondria, causes a small reduction in the VO_2 slow component without altering the initial VO_2 kinetics.²⁸ Similarly, and more practically, sodium bicarbonate ingestion reduces the VO_2 slow component during severe exercise without speeding the early VO_2 response (Figure 2).²⁹ In the latter case, a greater efflux of H^+ from muscle might retard the rate of fatigue development and delay the recruitment of less-efficient type II fibers. Most recently, increased dietary nitrate consumption has been reported to result in a reduced O_2 cost for a fixed moderate-intensity work rate and a reduced VO_2 slow component and increased time to exhaustion at a fixed severe-intensity work rate.³⁰ This effect is likely mediated through conversion of nitrate to nitrite and thence to nitric oxide, a potent vasodilator and modulator of mitochondrial function.

Other interventions that influence VO_2 kinetics are either illegal or impractical for enhancing sports performance. Erythropoietin administration significantly increases hemoglobin concentration and $\text{VO}_{2\text{max}}$ (and thus exercise performance) but does not alter VO_2 kinetics in any intensity domain (Figure 2).³¹ Acute plasma volume expansion results in a small increase in $\text{VO}_{2\text{max}}$ and improves high-intensity exercise performance but also without affecting either the initial fast component or subsequent slow component VO_2 responses.³² Conversely, the withdrawal of 450 mL of whole blood reduces $\text{VO}_{2\text{max}}$ and improves high-intensity exercise performance without appreciably altering the VO_2 kinetics.³³ The fact that these interventions, which would be expected to alter bulk muscle O_2 delivery, do not significantly affect VO_2 kinetics suggests that factors intrinsic to the muscle cells

are chiefly responsible for regulating the VO_2 response to exercise, at least in young healthy participants.⁴ On the other hand, the inspiration of a hyperoxic gas mixture significantly reduces the VO_2 slow component and enhances exercise tolerance.³⁴ In this case, an increased capillary PO_2 might reduce the rate of muscle fatigue development and reduce the requirement for lower-efficiency muscle fibers to be recruited as high-intensity exercise proceeds.^{10,11}

Conclusions

The adaptation of VO_2 following the onset of exercise of different intensities can have an impact on the muscle metabolic milieu and thus influence exercise performance. In the opinion of the authors, athletic performance capacity cannot be fully understood without knowledge of the VO_2 kinetics and its interaction with other parameters of aerobic function. Although much remains to be understood concerning the fundamental control of, and the constraints on, VO_2 kinetics, there is a growing awareness among coaches and sports physiologists of the role played by VO_2 kinetics in shaping exercise tolerance. Additional applied research is now required to translate existing knowledge into interventions with the potential to enhance sports performance.

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