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Research article

Oxygen uptake kinetics during incremental- and decremental-ramp cycle ergometry

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Abstract

The pulmonary oxygen uptake (VO_2) response to incremental-ramp cycle ergometry typically demonstrates lagged-linear first-order kinetics with a slope of ~10-11 $ml \cdot min^{-1} \cdot W^{-1}$, both above and below the lactate threshold (θ_L), i.e. there is no discernible VO_2 slow component (or "excess" VO_2) above θ_L. We were interested in determining whether a reverse ramp profile would yield the same response dynamics. Ten healthy males performed a maximum incremental -ramp (15-30 $W \cdot min^{-1}$, depending on fitness). On another day, the work rate (WR) was increased abruptly to the incremental maximum and then decremented at the same rate of 15-30 $W.min^{-1}$ (step-decremental ramp). Five subjects also performed a sub-maximal ramp-decremental test from 90% of θ_L. VO_2 was determined breath-by-breath from continuous monitoring of respired volumes (turbine) and gas concentrations (mass spectrometer). The incremental-ramp VO2-WR slope was 10.3 ± 0.7 $ml \cdot min^{-1} \cdot W^{-1}$, whereas that of the descending limb of the decremental ramp was 14.2 ± 1.1 $ml \cdot min^{-1} \cdot W^{-1}$ ($p < 0.005$). The sub-maximal decremental-ramp slope, however, was only 9.8 ± 0.9 $ml \cdot min^{-1} \cdot W^{-1}$: not significantly different from that of the incremental-ramp. This suggests that the VO_2 response in the supra-θ_L domain of incremental-ramp exercise manifest not actual, but pseudo, first-order kinetics.

Key words: Oxygen uptake-work rate gain, incremental-ramp exercise, decremental-ramp exercise, system linearity.

Introduction

The magnitude and profile of the pulmonary oxygen uptake (VO_2) response during incremental-ramp cycle ergometry are widely used as characteristics of the determinants of exercise tolerance in humans, i.e. its gain ($\Delta VO_2/\Delta WR$), response time constant and its maximum (e.g. Whipp et al., 1981). Typically, at all but extremely slow incrementation rates (Hansen et al., 1988; Whipp and Mahler 1980; Zoladz et al. 1995), the VO_2 response to such tests demonstrates the lagged-linear behaviour characteristic of first-order kinetics, with the VO_2 'lag', relative to steady-state VO_2 requirement for that work rate (WR), reflecting the mean response time (MRT) for the kinetics (Linnarsson, 1974; Hughson and Morrissey, 1982), as schematised in Figure 1a.

The gain of the VO_2 response during incremental-ramp exercise has been shown not to differ significantly from that of its steady-state O_2 cost for cycle ergometry (Whipp et al., 1981), with values of ~ 9-11 $ml \cdot min^{-1} \cdot W^{-1}$ (e.g. Davis et al., 1982; Hansen et al., 1984; Neder et al., 1999; Whipp et al., 1981), thereby allowing work efficiency to be estimated. While this is the expected VO_2 profile for a system expressing linear first-order kinetics, it is surprising that this lagged-linear response is conserved during exercise above θ_L where, at least for constant-WR exercise, VO_2 is known to diverge from dynamic system linearity (Hughson and Inman, 1986; Jones and Poole, 2005; Whipp et al., 1981; Yano et al., 2003).

These features of the incremental-ramp VO_2 profile might suggest that, in response to a symmetrical mirror-image ramp WR profile (i.e. a step-decremental ramp), a similarly-apparent first-order VO_2 kinetic response would result, as schematized in Figure 1b. However, we had noticed (Whipp et al., 1992) that when we imposed such a mirror-image ramp WR profile, the VO_2 response was not that implicit from the incremental-ramp behaviour. Rather, the slope of the decremental-ramp VO_2 response was appreciably greater.

Yano et al. (2004) demonstrated, from a detailed series of studies, that the group-mean VO_2 slope response of their subjects to decremental-ramp exercise, imposed from a particular absolute high-intensity constant-WR background, was also significantly greater than that in response to incremental exercise of the same WR profile - but of reverse sign. This differed from our previous study (Whipp et al., 1992), in that we utilized the entire incremental tolerance limit and with its mirror-image profile not imposed on a control period with a developing slow phase of the VO_2 kinetics (VO_2sc).

We were therefore interested both in determining whether the different features of the VO_2 responses to incremental and decremental WR ramps is a consistent feature in individual subjects over the entire tolerance range and what further insights such differences might provide with respect to the control mechanisms for the kinetics of VO_2 during high-intensity exercise.

Methods

Subjects and procedures

Ten healthy, recreationally-active male volunteers (age 31 ± 12 yr; weight 71 ± 8 kg; height 1.77 ± 0.08 m; peak VO_2 (VO_{2peak}) 3.56 ± 0.59 $l \cdot min^{-1}$) participated in the study, with each having provided written informed consent. The investigation was approved by the St. George's Hospital Research Ethics Committee, with procedures being con-

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ducted in accordance with the Declaration of Helsinki. Prior to testing, the subjects were familiarised with the equipment, procedures and laboratory personnel and, for the 24 hr prior to each testing session, were requested to refrain from participating in strenuous exercise.

Equipment

The tests were performed on a computer-controlled, electromagnetically-braked cycle ergometer with WR being independent of cycling cadence (Excalibur Sport, Lode, NL). The subjects breathed through a mouthpiece connected to a low-dead space (90 ml), low resistance (<1.5 cm H_2O at 3 $L{\cdot}s^{-1}$) turbine volume transducer (Interface Associates, Irvine, CA, USA) for the measurement of inspiratory and expiratory airflow and volume; calibration was performed manually with a 3 L syringe (Hans Rudolph, Kansas City, MO, USA) using flow profiles that spanned the experimental range. Respired gas was continuously sampled at 1 $ml{\cdot}s^{-1}$ from the mouthpiece and analysed by a quadrupole mass spectrometer (QP9000, Morgan Medical, Gillingham, UK) for [O_2], [CO_2] and [N_2]; calibration was performed using two precision-analysed gas mixtures that spanned the inspiratory-expiratory concentration range. Immediately after each test, the calibration gas mixtures were re-sampled to verify the stability of the calibration. The time delay between the volume and gas concentration signals was measured by passing a bolus of high-CO_2, low-O_2 gas through the system using a solenoid valve (Beaver et al., 1973) which was then used to phase-align the signals. Following analogue-to-digital conversion, the electrical signals from these devices were sampled and digitised every 20 ms by computer for breath-by-breath determination of ventilatory and gas exchange variables using the algorithms of Beaver et al. and Jenkins et al. (Beaver et al., 1973; Jenkins et al., 1989). The calibration and validation procedures have been described previously (Beaver et al., 1981). Throughout each test, arterial O_2 saturation and heart rate were measured using pulse oximetry (Biox 3745, Ohmeda, Louisville, USA) and the R-R interval of the electrocardiogram (Quest, Burdick, Washington, USA), respectively.

Exercise protocols

Exercise tests in a given subject were performed on different days. All tests were preceded (≥ 4 min) and followed (≥ 6 min) by a 20 W baseline.

Incremental-ramp test. Subjects first completed an incremental-ramp test (Figure 1a; 15-30 $W{\cdot}min^{-1}$; the chosen WR incrementation rate depending on subject fitness) to the limit of tolerance for: (a) determination of VO_{2peak}, taken to be the mean VO_2 for an integral number of breaths over the final 20 s of the incremental phase; (b) non-invasive estimation of the lactate threshold (θ_L), using standard ventilatory and gas-exchange criteria (Beaver et al., 1986; Whipp et al., 1986); and (c) the VO_2-WR profile.

Decremental-ramp test. A maximal decremental-ramp test (Figure 1b was conducted to allow comparison of the VO_2-WR profile with that for the incremental-ramp test. This was a mirror image of the incremental-ramp test: i.e. after an initial 20W baseline phase, the WR was increased abruptly to the maximum attained on the incremental-ramp test (WR_{max}) and then decremented back to the 20W baseline at the same rate as that of the incremental-ramp test (i.e. 15-30 $W{\cdot}min^{-1}$). A subgroup of the subjects (n = 5) also completed a sub-maximal decremental-ramp test (Figure 1b), which resembled the maximal decremental-ramp test, except that the WR was initially increased only to 90% of θ_L before being decremented back to 20W at the appropriate individual slope of 15-30 $W.min^{-1}$. This allowed comparison of the VO_2-WR profile with that of both incremental-ramp and the maximal decremental-ramp tests.

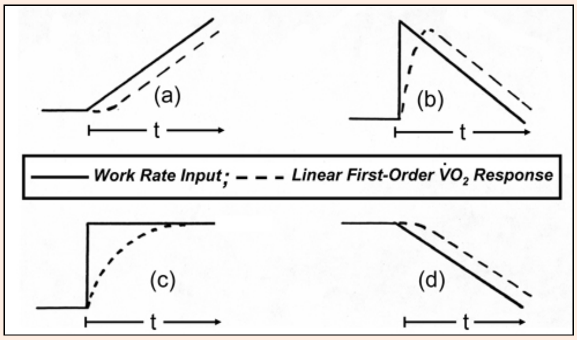

Figure 1. Schematic representation of linear first-order O_2 uptake (VO_2) responses as a function of time (- - -) for (a) an incremental ramp exercise test, (b) a step-decremental ramp exercise test, (c) a step (or constant work-rate) exercise test and (d) a decremental ramp exercise test. The work rate profiles are shown as solid lines. See text for further detail.

Constant-WR test. The subjects also completed at least three sub-θ_L constant-WR tests (Figure 1c; as determined from the incremental-ramp test), from a 20W baseline, each of 6 min duration, in order to establish the steady-state VO_2-WR relationship.

Data analysis and statistics

The breath-by-breath VO_2 data were edited to eliminate occasional breaths triggered by, for example, swallows, coughs or sighs which were considered to be uncharacteristic of the underlying physiological response; only breaths > 4 SD of the local mean being excluded (Lamarra et al., 1987). The baseline VO_2 was taken as the mean VO_2 for an integral number of breaths over the last 60 s of the 20 W baseline. The slope of the linear phase of the VO_2-WR response for incremental-ramp and decremental-ramp tests was obtained by least-squares regression analysis (Origin, Microcal, USA).

A Student's *t*-test was used to compare the slopes of the VO_2-WR regression lines across the different test types. Differences were considered significant if $p < 0.05$. The dispersion about the mean is expressed as ± standard deviation (SD), unless otherwise specified.

Results

A representative example of the VO_2 response profile for the incremental-ramp test is shown in Figure 2a, with the dashed line indicating the response slope over the linear region of the response; the solid circles are the steady-

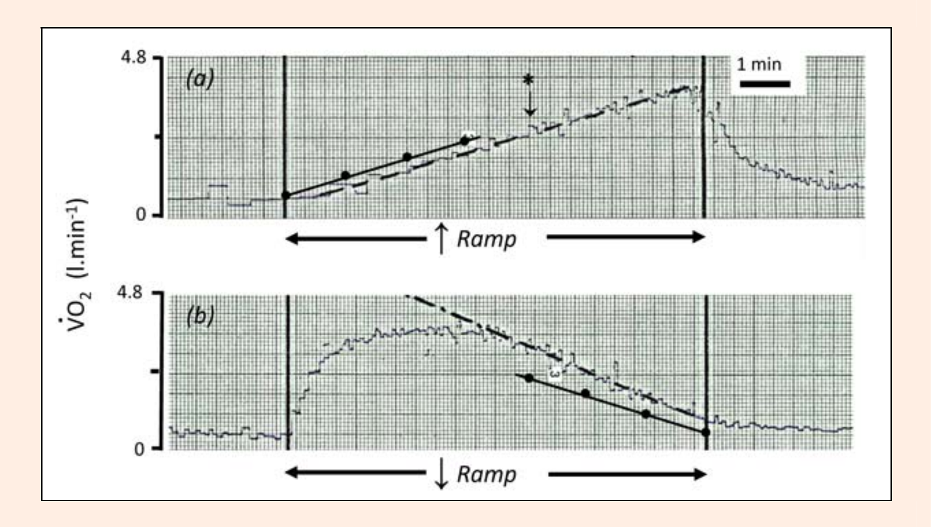

Figure 2. Breath-by-breath VO_2 responses as a function of time in a representative subject for (a) incremental-ramp exercise (↑ Ramp; 30 $W.min^{-1}$) and (b) maximal decremental-ramp exercise (↓ Ramp; 30 $W{\cdot}min^{-1}$). Asterisk represents θ_L. Solid circles represent steady-state responses, with line of best fit (solid line). Lines of best fit to the linear regions of the incremental and decremental ramp responses are shown as dashed lines.

state requirements, determined from the 6-min constant-WR tests. The mean incremental-ramp VO_2 slope ($\Delta VO_2/\Delta WR$) was 10.26 ± 0.70 $ml{\cdot}min^{-1}{\cdot}W^{-1}$ with a range of 9.0-11.2 $ml{\cdot}min^{-1}{\cdot}W^{-1}$ (Figure 3, solid circles). This response slope was not significantly different from that of the steady-state sub-θ_L VO_2 response. However, this 'apparently' first-order VO_2response for the incremental ramp was not evident in the decremental-ramp profile (e.g. Figure 2b). The VO_2 slope was appreciably and significantly steeper than that of the incremental-ramp test, i.e. $\Delta VO_2/\Delta WR$ averaging 14.16 ± 1.02 $ml.min^{-1}.W^{-1}$ with a range of 12.7-15.5 $ml{\cdot}min^{-1}{\cdot}W^{-1}$ (Figure 3, open circles; $p < 0.005$).

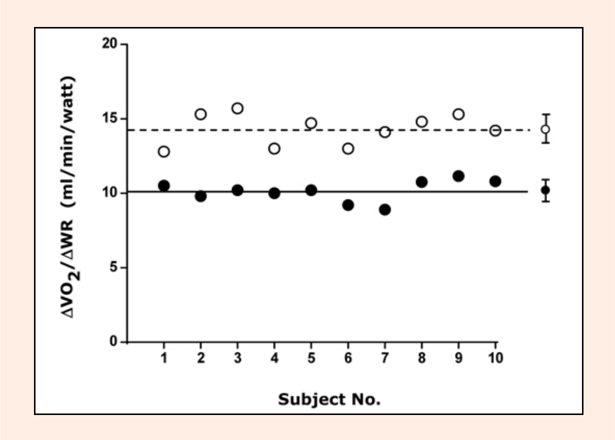

Figure 3. Individual subject VO_2-WR slope ($\Delta VO_2/\Delta WR$) responses for incremental-ramp exercise (solid circles) and maximal decremental-ramp exercise (open circles); solid and dashed lines, with error bars, represent the respective mean ± standard deviation ($p < 0.005$).

To determine whether this was a standard feature for *any* decremental ramp forcing, five of the subjects also performed a submaximal decremental-ramp test such that the peak WR of the decremental ramp was at 90% of θ_L. A representative example of the sub-θ_L decremental ramp VO_2 response (open circles), together with the corresponding maximal decremental ramp response (crosses) is presented in Figure 4. In each subject, the VO_2 slope (open triangles) (Figure 5) was clearly not as steep as that for the maximal decremental-ramp test (Figure 3, open circles), $\Delta VO_2/\Delta WR$ averaging 9.84 ± 0.90 $ml{\cdot}min^{-1}{\cdot}W^{-1}$ and ranging between 8.2 and 10.7 $ml{\cdot}min^{-1}{\cdot}W^{-1}$. This was significantly different from the maximal decremental-ramp $\Delta VO_2/\Delta WR$ ($p < 0.005$) but not from the incremental ramp value (Figure 5, solid circles).

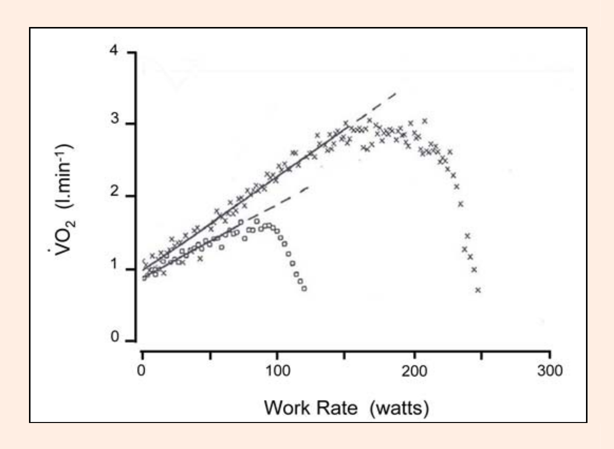

Figure 4. Breath-by-breath VO_2 responses as a function of work rate, displayed as mirror images, in a representative subject for: maximal decremental-ramp exercise (crosses) and sub-maximal decremental-ramp exercise (open circles). The dashed lines are the lines of best fit over the linear regions of the decremental VO_2 response.

Discussion

The concept of superposition with respect to dynamical systems analysis would suggest that the profile of a first-order dynamic VO_2 response to muscular exercise would be predictable, regardless of the dynamic forcing regime employed (e.g. Fujihara et al., 1973; Whipp and Ward, 1981). And so the VO_2 response to the decremental ramp, performed as a mirror-image of the incremental profile, and importantly over the same time frame, might be expected to yield similar response kinetics. That is, in a dynamically-linear system the VO_2 response should decrease with the linear profile (after the initial kinetic lag period) equivalent to that expressed by the ramp-incremental test as schematised in Figure 1. It did not, in any of our subjects!

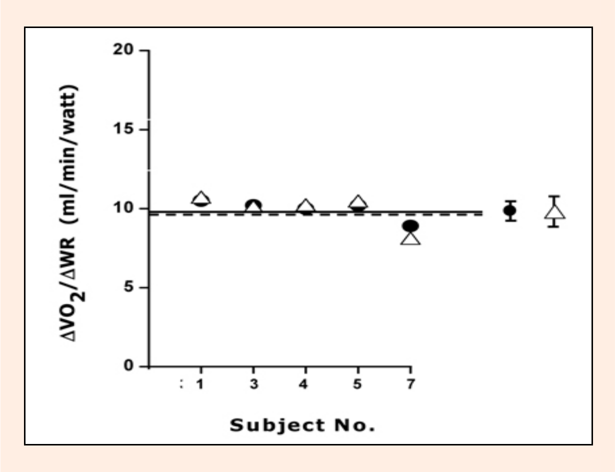

Figure 5. **Individual subject $VO_{2\text{-}WR}$ slope ($\Delta VO_2/\Delta WR$) responses for incremental-ramp exercise (solid circles) and sub-maximal decremental-ramp exercise (open triangles); solid and dashed lines, with error bars, represent the respective mean ± standard deviation.**

However, the VO_2 response profile to the decremental ramp should, we believe, be considered in the context of the more widely investigated incremental ramp. That is, if, as previously demonstrated (Davis et al., 1982; Hansen et al., 1984; Hughson and Inman, 1986; Whipp et al., 1981), the VO_2 response to the incremental-ramp tests over the sub-θ_L region is characteristic of the first-order gain expressed in constant-WR tests over the same intensity range, then the retained linearity over the supra-θ_L region may also be considered consistent with these first-order features; i.e. the same rate of change of work rate yielding the same rate of change of VO_2. Similar to previous studies using ramp-incremental exercise of these durations, there was no evidence in any of the participants in this study (e.g. Figure 2) of an "excess" VO_2 (or slow component of VO_2). If present, this would be expected to be manifest as a curvilinear increase in the VO_2 response in the supra-θ_L region. However, as the slow component of the VO_2 kinetics has been shown to be both slow and of delayed onset (Barstow and Molé, 1991; Linnarsson, 1974; Paterson and Whipp, 1991; Perrey et al., 2001; although see Stirling and Zakynthinaki (2009) for a dissenting viewpoint on the delay characterization), we propose that its influence during rapidly-incremental ramp tests is virtually undetectable; not beginning until a work rate beyond the subject's θ_L and then developing slowly over the remaining, and relatively short, work-rate region. This has also been shown to be the case for constant-WR tests of sufficiently high intensity that the subject reaches the maximum VO_2 in about 3-4 minutes (e.g. Özyener et al., 2001; Burnley and Jones, 2007).

The inference that the continued linearity of the supra-θ_L VO_2response for incremental-ramp exercise reflects first-order behaviour, however, presupposes that the steady-state VO_2 response in this range likewise remains linear. This is not the case for supra-θ_L constant-WR exercise, there being a supplemental increase in VO_2 (i.e. VO_2sc) which increases the O_2 cost of the exercise above that expected for the wholly-aerobic VO_2 progression, as demonstrated initially by Whipp and Mahler (1980) and subsequently by others (e.g. Barstow and Molé, 1991; Zoladz et al., 1997; Burnley et al. 2000) – the gain of the fundamental component of the VO_2 response, however, is either not, or not appreciably, altered (Barstow and Molé, 1991; Jones and Poole 2005; Özyener et al., 2001; Paterson and Whipp 1991). It is of interest, therefore, that very slow WR incrementation rates can result in a VO_2 response in the supra-θ_L region that is concave upwards (Hansen et al., 1988; Zoladz et al., 1995, Whipp and Mahler 1980), presumably reflective of the VO_2sc having sufficient time to be expressed. Consequently, the VO_2 response pattern in this supra-θ_L domain of the incremental-ramp appears to manifest not actual but, what might be termed, pseudo-first-order kinetics.

In contrast, a VO_2 response consistent with an "excess" component was clearly demonstrable in each of our subjects during the maximal decremental-ramp (e.g. Figures 2 and 5): in general agreement with the work of Yano et al. (2004; 2007). One difference between our findings and those of Yano and colleagues is that we did not see a "breakpoint" in the decremental VO_2 response at which the VO_2 slope was reduced at or near the subject's θ_L. In the study of Yano et al. (2004), however, the work-rate decrement began at the same absolute peak work rate, rather than at the individual maxima achieved during the incremental ramp (i.e. a maximal mirror-image symmetry), despite the differences in aerobic fitness of the participants. This difference in methodology between Yano et al. (2004) and the present study, therefore, may have contributed to the differences in the VO_2 response profile during the decremental-ramp protocol.

The major difference in the metabolic challenge to the maximal decremental work-rate profile, compared to that of the incremental ramp is that: (a) the proportion of type II muscle fibers contributing to the force generation is maximized from exercise onset and then decreases progressively in concert with the work rate – although we are not aware of any studies that have characterised the fiber-type contribution to this kind of exercise, and so our supposition is based on the profiles to increases in work rate; and (b) the anaerobic-glycolytic supplementation to the aerobic component of the energy transfer begins at, or shortly following, the onset of the exercise and with a maximal contribution.

As the lactate production rate is likely to increase to high levels almost immediately, the presence of an "excess" VO_2 component with the maximal decremental-ramp exercise is, plausibly, consistent with the increased O_2 cost of metabolizing the lactate. Any lactate that is "cleared" to CO_2 and H_2O in non-lactate producing fibers will incur only a relatively small, if any, additional VO_2 cost, i.e. the reduction in glycolytic ATP yield in the fiber(s) (or other tissues) clearing the lactate will be offset by the actual ATP yield in the fibers producing it. The regeneration of depleted glycogen will, of course, have an obligatory and additional VO_2 cost. However, it is hard to conceive of a significant hepatic component associated with exercise of this duration: repletion presupposes a prior depletion. It also seems unlikely that a muscle fiber that is producing lactate, and hence to some extent depleting its glycogen reserves, will simultaneously reverse the process. However, a fiber that has been producing lactate and then stops contracting in order to reduce the force-generating requirements of the decremental ramp will have the potential to regenerate any glycogen reduction - with its associated increase in VO_2 cost.

An additional, or alternative, source of the high VO_2 cost of decremental ramp exercise may arise from an early onset of muscle fatigue consequent to the high degree of muscle requirement (of, presumably, all fibre types) from ramp onset. It has been suggested that muscle fatigue is necessary to generate the VO_2sc (Cannon et al., 2011; Poole et al., 1994). Intriguingly, whether the high VO_2 cost derives from the recruitment of type II muscle fibres (that are less-efficient, and/or have a high O_2 cost of force production) or from the consequences of fatigue in type I fibres (Cannon et al., 2011; Hepple et al., 2010; Nagesser et al., 1993; Zoladz et al., 2008) remains to be established. The latter may cause an increase in the abundance of type I fibres with cross-bridges in the force-generating state that resist filament sliding (particularly during relaxation), which could result in an increase in the energy (and O_2) cost of force production (Barclay, 1996; and see Jones et al., 2011 for review).

The precise mechanisms contributing to the additional VO_2 cost in the decremental ramp, therefore, remain to be elucidated. That it is lactate- and/or fatigue-associated, if not lactate-mediated, is supported by the results of Yano et al. (2003; 2004) and of our finding that when the work-rate peak of the decremental ramp was below the subject'sθ_L, the gain of the VO_2 response was consistent with a first-order response typical of constant work-rate tests in the same intensity domain.

Conclusion

The mechanisms for the different dynamic VO_2 response behaviour between incremental and decremental ramps remains to be resolved, with different profiles for fibre type recruitment, muscle fatigue and/or different pathways of lactate clearance being likely to be contributory. Regardless, the VO_2 response pattern in this supra-θ_L domain of incremental-ramp exercise appears to manifest not actual but what might be termed pseudo-first-order kinetics.

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Key points

- The slope of the decremental-ramp response is appreciably greater than that of the incremental.
- The response dynamics in supra-θ_L domain of the incremental-ramp appear not manifest actual first-order kinetics.
- The mechanisms underlying the different dynamic response behaviour for incremental and decremental ramps are presently unclear.

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