INVITED PAPER

SPECIAL ISSUE: ASSESSMENT AND INTERPRETATION OF YOUTH AEROBIC FITNESS

Oxygen uptake kinetics in youth: Characteristics, interpretation and application

Abstract

Pulmonary oxygen uptake ($\dot{V}O_2$) kinetics, which describe the aerobic response to near instantaneous changes in metabolic demand, provide a valuable insight into the control and coordination of oxidative phosphorylation during exercise. Despite their applicability to the highly sporadic habitual physical activity and exercise patterns of children, relatively little is known regarding the influence of internal and external stimuli on the dynamic $\dot{V}O_2$ response. Whilst insufficient evidence is available during moderate intensity exercise, an age-related slowing of the phase II time constant (τ) and augmentation of the $\dot{V}O_2$ slow component appears to be manifest during heavy intensity exercise, which may be related to changes in the muscle phosphate controllers of oxidative phosphorylation, muscle oxygen delivery and utilisation and/or muscle fibre type recruitment patterns. Similar to findings in adults, aerobic training is associated with a faster phase II τ and smaller $\dot{V}O_2$ slow component in youth, independent of age or maturity, indicative of an enhanced oxidative metabolism. However, a lack of longitudinal or intervention-based training studies limit our ability to attribute these changes to training *per se*. Further, methodologically rigorous studies are required to fully resolve the interaction(s) between age, sex, biological maturity and external stimuli, such as exercise training and exercise intensity, and the dynamic $\dot{V}O_2$ response at the onset and offset of exercise.

Introduction

Pulmonary oxygen uptake ($\dot{V}O_2$) kinetics following the onset of constant-work-rate exercise provide a useful assessment of the integrated capacity of the organism to transport and utilize O_2 to support the increased rate of energy turnover in the contracting myocytes (107). The onset of exercise, or an increase in exercise intensity, engenders an elevated energetic demand. Transiently, this is met by intramuscular phosphocreatine (PCr) degradation and the anaerobic catabolism of glycogen. However, $\dot{V}O_2$ simultaneously rises in an exponential manner (52, 53), thereby enabling a progressively greater proportion of the energetic demand to be met by oxidative phosphorylation.

Pulmonary $\dot{V}O_2$ response profiles

The pulmonary $\dot{V}O_2$ response following the onset of exercise has been extensively characterised across many different exercise modalities (e.g. 27, 59, 93). The three-phase pulmonary $\dot{V}O_2$ response, first reported by Whipp and Wasserman (109), consists of an initial rapid increase in $\dot{V}O_2$ at the onset of exercise that is typically initiated within the first breath. During this phase, termed the cardiodynamic phase or phase I, pulmonary and muscle $\dot{V}O_2$ are temporally dissociated due to the muscle-lung transit delay. Furthermore, the amplitude of the $\dot{V}O_2$ at the muscle and mouth differ due to oxygen (O_2) stores within the body and an increasing cardiac output (107, 108). This dissociation between muscle and pulmonary $\dot{V}O_2$ is evident in the response profiles as the cardiodynamic phase is only present in the pulmonary $\dot{V}O_2$ response (Figure 1); muscle $\dot{V}O_2$ increases in a mono-exponential fashion from the onset. Provided this initial cardiodynamic phase is appropriately accounted for, the subsequent muscle and pulmonary $\dot{V}O_2$ responses demonstrate a close agreement in both the time course and amplitude of the $\dot{V}O_2$ response (within +/- 10%: 13, 49).

The cardiodynamic phase of the pulmonary $\dot{V}O_2$ response is succeeded by an exponential increase in $\dot{V}O_2$, known as phase II, which drives the $\dot{V}O_2$ towards the actual, or originally projected, steady state. The rate at which this exponential increase in $\dot{V}O_2$ occurs is described by the time constant (τ), which reflects the time taken to achieve 63% of the phase II response (For a review of modelling approaches, see: 38, 89). As illustrated in Figure 2, during moderate intensity exercise below the gas exchange or lactate threshold (GET/LT), phase II is followed by the attainment of a steady state (phase III), typically in 2-3 minutes, where O_2 demands and utilisation are matched (60).

Exercise intensities above the GET but below critical power (CP) are described as within the heavy intensity domain. Whilst this exercise intensity is associated with an elevated blood lactate concentration, a muscle metabolic steady state is attainable (105). In children, critical power is reported to occur at 65-80% peak $\dot{V}O_2$ (37, 44), with this range suggested to be likely to be methodological rather than metabolic in nature (18).

In adults, heavy intensity exercise is further characterised by the presence of a slow component which becomes apparent after 90-150 seconds (14, 88) and delays the attainment of a steady state. Although it remains debated whether the slow component begins at the onset of exercise (72, 74) or develops after approximately two minutes (14, 16, 88), it is clear that the influence of the slow component is to elevate the $\dot{V}O_2$ above the steady state $\dot{V}O_2$ projected from extrapolation of the response to moderate intensity exercise. Whether a slow component is present in children's responses to heavy intensity exercise has been a matter of debate, with early work suggesting no slow component was present (1, 111). In contrast, more recent work has generally shown a slow component to be evident during both heavy and severe intensity exercise (39, 41, 85), albeit of a reduced amplitude compared to adults, irrespective of exercise modality (75, 81, 112). No studies have investigated the $\dot{V}O_2$ kinetic response to extreme intensity exercise (exercise in which fatigue occurs before peak $\dot{V}O_2$ can be attained (54)) in children but a $\dot{V}O_2$ slow component is unlikely to be manifest given reports in adults (110).

Linear, first order behaviour of $\dot{V}O_2$ kinetics

A linear, first order system obeys the law of superposition whereby the key response parameters (τ and the primary component gain) to a higher work rate can be predicted from the response to a lower work rate. Conventionally, in adults, the $\dot{V}O_2$ kinetic response within the moderate intensity domain was suggested to be independent of the relative work rate (49, 73, 106), but more recent work has challenged this notion (e.g. 26, 76), with suggestions that the $\dot{V}O_2$ τ may be work rate dependent in those characterised by a slower dynamic $\dot{V}O_2$ response (101). Indeed, a similar divergence from linear first order behaviour has been suggested by reports of a slower phase II τ during heavy than moderate intensity exercise in adults (58, 64, 88), although it is pertinent to note that not all findings agree with this contention (e.g. 14, 27, 86). Whether the $\dot{V}O_2$ kinetic response demonstrates first order behaviour in children remains to be elucidated, with no studies specifically investigating the influence of exercise intensity, within or between domains, on the $\dot{V}O_2$ kinetic response. Nonetheless, within study comparisons of the τ derived from moderate and heavy intensity exercise transitions appear to indicate that children's responses are independent of the work rate imposed (80).

Resolution of the dynamic linearity of the $\dot{V}O_2$ kinetic response across the continuum of exercise intensities is relevant to the elucidation of the factors regulating $\dot{V}O_2$ kinetics (64) which are complex, multifaceted and likely to be further mediated by factors such as age, exercise modality, training status and the environmental conditions. Poole et al. (90) suggested a 'tipping point' hypothesis with regard to the predominant determinants of the dynamic $\dot{V}O_2$ response. According to this hypothesis, healthy children and adults are likely to lie in the delivery-independent region of the tipping point during upright moderate intensity exercise, but certain perturbations, such as disease or hypoxic gas inspiration, may shift them to the O_2 delivery dependent region. A slowing of the phase II τ during heavy compared with moderate intensity exercise has been interpreted as reflective of a reduced O_2 availability (56). However, others have suggested that such a slowing may be attributable to a greater contribution of type II muscle fibres to meeting the higher exercise demands during heavy intensity exercise (58); type II fibres are

characterised by a slower phase II τ in isolated rodent muscles (67) and individuals with a greater proportion of type II fibres in the vastus lateralis demonstrate a slower phase II τ in adults (94). The determinants of the $\dot{V}O_2$ kinetic response in youth largely remains to be elucidated, although the majority of the evidence appears to support an intracellular limitation to O_2 utilisation rather than an O_2 delivery limitation in healthy children during upright exercise (81, 112).

Recovery of pulmonary $\dot{V}O_2$ kinetics following exercise

By comparison to the on transition, the $\dot{V}O_2$ recovery kinetics, which closely reflect muscle PCr kinetics (6, 97), have received considerably less attention and the appropriate characterisation of the $\dot{V}O_2$ recovery kinetics remains unclear. Specifically, in adults, there are contradictory findings regarding the mono- or bi-exponentiality of the response profile (20, 31, 35, 87), as well as the relative speed of the recovery response compared to the on-response (20, 48, 87, 88). In youth, the limited evidence available suggests a mono-exponential decline (6, 69, 82, 115) which is slower than (6, 69, 115) or similar to (77, 82) the respective $\dot{V}O_2$ on-response. It is interesting to note the findings of Marwood et al. who suggested that training may influence on-off symmetry (77); whilst this was not reported in other training status studies in youth (82), similar findings have been reported in adults (47).

Influence of age on pulmonary $\dot{V}O_2$ kinetics

In contrast to the extensive evidence regarding peak $\dot{V}O_2$, relatively few studies have considered the pulmonary $\dot{V}O_2$ response in paediatric populations, with many of those that have subject to fundamental methodological limitations. This has resulted in considerable heterogeneity between findings and little consensus in terms of the influence of age, maturity or sex on the dynamic $\dot{V}O_2$ response.

Very little is currently known regarding the amplitude and duration of phase I in youth, not least due to the small signal to noise ratio and influence of the baseline activity from which the transition occurs, both of which serve to preclude the reliable identification of the onset of phase II. Indeed, due to these

issues, the majority of paediatric studies have assumed a phase I duration of 15-25 s, subsequently deleting this part of the response from subsequent analyses. Although comparable studies have not been conducted in youth populations, it is pertinent to note a recent findings that assuming a shorter phase I duration than that experimentally determined has greater consequences on the subsequently derived phase II τ than assuming longer durations in both young and older adults (84). Caution is therefore required when making inter-study comparisons between those that have eliminated different durations of phase I from the data analysis. One of the few paediatric studies to visually identify the duration of phase I reported that it was less than 20 s during both moderate and severe intensity exercise in healthy children, suggesting that the utilisation of a 20 s period is appropriate (98).

Two early studies investigating the influence of age on the relative contribution of phase I to the end-exercise amplitude during moderate intensity exercise reported this to be similar (29) or lower (102) in children than adults when the phase I duration was assumed to be 20 s and 15 s, respectively. However, given the dependence of phase I on the cardiac output kinetics at the onset of exercise (68, 113), and the age-related increase in the cardiac output required for a given pulmonary $\dot{V}O_2$ (103), potentially due to differences in absolute muscle mass involved, the appropriateness of a set phase I duration across the age range should be questioned. Indeed, Hebestreit et al. (51) found that whilst the phase I duration remained stable in boys aged 9 to 12 years across a range of exercise intensities, similar exercise was associated with a negative relationship between age and phase I duration in adult males aged 19-27 years. A subsequent longitudinal study reported that during heavy intensity exercise phase I increased in duration by ~3s between 11-13 years of age (Boys: 16.7 ± 3.3 to 19.5 ± 3.0 s; Girls: 20.7 ± 4.7 to 24.3 ± 6.1 s; 40).

On the basis of early studies that reported no differences in the dynamic $\dot{V}O_2$ response to moderate intensity exercise between children and adults, it was suggested that the phase II response was fully mature by early childhood and independent of sex. However, more recent, methodologically robust studies re-examining the influence of age have reported contradictory findings, with a faster phase II τ

evident in children than adults (43, 71). It is likely that this discrepancy is attributable to a failure of earlier studies to utilise well-defined and adequately powered sample populations and to use appropriate modelling and data averaging techniques (7). Indeed, an age-related slowing of the $\dot{V}O_2$ kinetic response agrees with evidence from both longitudinal and cross-sectional studies which consistently report an increased τ and magnitude of the $\dot{V}O_2$ slow component with age during heavy intensity exercise, irrespective of sex (25, 40, 111).

Mechanistic basis for age-related changes in pulmonary $\dot{V}O_2$ kinetics

A number of factors have been suggested to be associated with the age-related differences in $\dot{V}O_2$ kinetics reported which may occur in combination or isolation depending on the exercise modality and intensity (7). The phosphocreatine-creatine (PCr-Cr) shuttle has been suggested to be a key rate limiting step in oxidative phosphorylation, a contention supported by the close kinetic coupling between the fall in muscle PCr and the exponential rise in pulmonary $\dot{V}O_2$ at the onset of moderate intensity exercise (6). It has subsequently been proposed that age-related changes in the muscle phosphate controllers (PCr and adenosine diphosphate (ADP)) may therefore contribute to the faster $\dot{V}O_2$ kinetics observed in youth than adults. However, direct evidence for this hypothesis is largely limited to early muscle biopsy studies which reported higher oxidative enzyme activity and lower PCr concentrations in children than adults (19, 50), although it is pertinent to note that some found no age related difference in muscle metabolism (17). More recent investigations using high resolution ^{31}P-magnetic response spectroscopy suggests that the role of muscle phosphate controllers may be exercise intensity dependent, with no differences observed in the rate of PCr decline at the onset of moderate intensity exercise between children and adults (10) but a lower fall in muscle PCr and pH in children during exercise above the GET (11, 114). These findings generally suggest a higher oxidative energy contribution during high intensity exercise in children, with a reduced reliance on substrate-level phosphorylation, agreeing with the recent suggestions that children are similar to endurance trained adults (96).

It has also been suggested that the slowing of $\dot{V}O_2$ kinetics with age may be attributable to an age-related reduction in muscle blood flow and thus O_2 delivery, with early studies reporting greater muscle blood flow after ischaemic and maximal intensity exercise in children (62, 63). Indeed, a slower phase II τ during hypoxic conditions (15% O_2) has been reported in children (102), demonstrating that the pulmonary $\dot{V}O_2$ response is sensitive to changes in O_2 delivery in children. Furthermore, a recent study demonstrated a close matching of the estimated capillary blood flow and pulmonary $\dot{V}O_2$ kinetics, both of which were faster in the children than adults (71). These findings may be indicative that the capillary blood flow kinetics limit the pulmonary $\dot{V}O_2$ kinetics and contribute to age-related differences in $\dot{V}O_2$ kinetics, although a faster O_2 extraction was also reported in the children which may reflect a greater oxidative capacity in children (71). To fully substantiate a role of O_2 delivery as a rate limiter in the $\dot{V}O_2$ kinetic response, evidence supporting a faster $\dot{V}O_2$ response under conditions in which O_2 delivery is enhanced is required. However, studies that have sought to increase O_2 delivery through the use of priming exercise have reported no speeding of the phase II τ in children and an amelioration of the $\Delta HHb/\Delta\dot{V}O_2$ ratio overshoot in bout 2, suggesting that the phase II τ in young boys may predominantly be limited by intramuscular metabolic factors rather than O_2 delivery (8, 9).

Alternatively, or additionally, the increasing phase II τ and magnitude of the $\dot{V}O_2$ slow component with age may be related to muscle fibre type recruitment, with type I muscle fibre type distribution positively and negatively associated with the phase II τ and $\dot{V}O_2$ slow component, respectively (12, 95). Indeed, in adults, a higher proportion of type I muscle fibres has been associated with faster muscle $\dot{V}O_2$ and PCr kinetics (30, 67), while ~85% of the $\dot{V}O_2$ slow component has been shown to originate in the contracting muscle (91) and to be associated with the recruitment of less efficient, higher-order type II muscle fibres (34, 66). Comparable data is not available in children but a role of muscle fibre type recruitment or proportions is supported by reports that the percentage distribution of type I fibres decreases from ~58 to 48% from 10 to 20 years of age in boys (57) and by the reduced accumulation of fatigue-inducing metabolites during high intensity exercise in children (11, 114) which would be anticipated to delay or preclude the recruitment of additional, potentially type II, muscle fibres.

However, a similar change in the proportion of muscle fibre types was not reported in girls (57) and findings from studies using iEMG found no change in muscle activation over the period during which the $\dot{V}O_2$ slow component was manifest, in contrast to adults (24). Similarly, results from a recent study using the transverse relaxation time derived from magnetic resonance imaging suggested that the $\dot{V}O_2$ slow component was independent of changes in muscle activation in boys, but not men (23). Taken together, these findings may be indicative that the progressive recruitment of muscle fibres during exercise becomes increasingly more important to meeting the exercise demand with age, leading to the greater $\dot{V}O_2$ slow component observed in adults. Indeed, when the recruitment of type II fibres was experimentally augmented in youth through altering the pedal cadence and baseline work rate (22, 24), a slower phase II τ was observed, demonstrating the sensitivity of pulmonary $\dot{V}O_2$ kinetics to muscle fibre type recruitment patterns in youth.

Influence of sex on pulmonary $\dot{V}O_2$ kinetics

Few studies have specifically investigated the influence of sex on the $\dot{V}O_2$ kinetics response and little consensus is presently available. Specifically, whilst Fawkner et al. (43) reported no sex differences in the $\dot{V}O_2$ kinetics of children or adults during moderate intensity cycling exercise, Franco et al. (46) reported faster $\dot{V}O_2$ kinetics in obese adolescent boys during treadmill exercise, although the use of a single exercise "transition" that was a posteriori identified as being of moderate intensity limits potential interpretation of the latter studies findings. During heavy intensity exercise, faster $\dot{V}O_2$ kinetics and a reduced $\dot{V}O_2$ slow component have been suggested in boys (40, 42); whether this difference is attributable to sex *per se* remains to be elucidated as the boys also demonstrated a higher peak $\dot{V}O_2$ so the faster τ may reflect a superior aerobic fitness in the boys, although it is pertinent to note that no association was reported between peak $\dot{V}O_2$ and the phase II τ in these studies, a finding similarly reported elsewhere (46, 80, 112). These apparent inter-study discrepancies may be attributable to the exercise intensities utilised, with heavy intensity exercise likely to shift the key determinants of the $\dot{V}O_2$ kinetic response towards a greater contribution of O_2 delivery. However, whilst boys demonstrate a

greater stroke volume during exercise, no sex differences in cardiac output for a given $\dot{V}O_2$ have been reported (103). Further studies which account for the potential mediatory roles of maturation and cardiorespiratory fitness are therefore required to fully elucidate the influence of sex and its interaction with exercise intensity.

Influence of training on pulmonary $\dot{V}O_2$ kinetics

In contrast to adults in whom training represents a potent stimulus to the dynamic pulmonary $\dot{V}O_2$ response, the earliest studies in prepubertal children indicated that the trained state was associated with neither a reduced phase II τ (28, 85) nor a reduced amplitude of the $\dot{V}O_2$ slow component (85). These findings are likely to be attributable to many of the methodological limitations already discussed, in addition to a lack of commonality between the training and testing modalities (28, 85). However, it was also suggested that these findings may reflect the presence of a maturational threshold below which a significant physiological response to training was not manifest (61). In contrast to this notion and the earlier studies, more recent, methodologically rigorous, studies report a significant influence of training status on the $\dot{V}O_2$ kinetics of both prepubertal children (80, 112) and pubertal adolescents (78, 81, 104), although these differences were still restricted to the temporal parameters with no influence of the magnitude of the $\dot{V}O_2$ slow component. Perhaps surprisingly given the relevance to training guidelines and performance (33), no studies have directly addressed the question of sex differences in the response of $\dot{V}O_2$ kinetics to training. Inter-study comparisons suggest that sex is unlikely to mediate the $\dot{V}O_2$ kinetic response to training, in agreement with reports of similar relative training induced adaptations in peak $\dot{V}O_2$ irrespective of sex (4), although it is pertinent to note that the mechanistic basis for such training adaptations may be sex-dependent, especially following the onset of puberty.

Longitudinal or intervention-based studies investigating the influence of training on the dynamic $\dot{V}O_2$ response are almost non-existent. Indeed, only one study has investigated the influence of a short-term, high intensity intervention in obese children, highlighting the potential utility of pulmonary $\dot{V}O_2$ kinetics, relative to traditional peak $\dot{V}O_2$ measures, in identifying the physiological impact of training.

Specifically, whilst the peak $\dot{V}O_2$ of obese children was not influenced, the dynamic pulmonary $\dot{V}O_2$ response to heavy intensity exercise was 20% faster following just 6 weeks of training (80). Interestingly, this magnitude of adaptation was similar to that previously observed in cross-sectional comparisons of trained and untrained pre-pubertal children (112).

Only two studies have sought to investigate the influence of training on the recovery pulmonary $\dot{V}O_2$ kinetics during youth, reporting largely contradictory findings. McNarry *et al*. (82) found training to be associated with a significantly faster pulmonary $\dot{V}O_2$ phase II τ in both prepubertal and pubertal swimmers, but Marwood *et al.* (77) observed no influence of training on pubertal soccer players.

Mechanistic basis for training-related changes in pulmonary $\dot{V}O_2$ kinetics

The mechanistic basis for training adaptations in children largely remains to be resolved, with potential conclusions with regards to the relative contribution of O_2 delivery and utilisation adaptations hampered by the inherently indirect techniques necessitated by the paediatric population and associated ethical constraints. Indeed, interpretations with regard to the influence of training on O_2 delivery are based on the tenuous extrapolation of heart rate kinetics to reflect muscle blood flow kinetics and/or convective O_2 transport (76). Specifically, the faster HR kinetics reported in both pre-pubertal (81) and pubertal (78, 82) athletes may be indicative of an enhanced O_2 delivery to the muscle enabling faster $\dot{V}O_2$ kinetics, in accord with studies in adults reporting faster conduit artery flow and vascular conductance following training (65, 100). However, it is important to note that increased bulk O_2 delivery in the trained state does not necessarily imply that O_2 availability was limiting in the untrained state. At the onset of exercise, Marwood *et al*. (78) and Unnithan et al. both found no effect of training on the [HHb] response in adolescent boys and girls, respectively, during moderate intensity exercise, whereas McNarry *et al.* (81) observed significantly faster [HHb] kinetics during heavy intensity exercise in trained adolescent girls. No studies have investigated the influence of training on the [HHb] response to the onset of exercise in pre-pubertal children. Following moderate intensity exercise, Marwood et al. (77) reported a significantly faster [HHb] recovery τ in trained adolescent boys whereas, following

heavy intensity exercise, McNarry et al. (82) reported no difference in girls according to training status, maturity or exercise modality, with the exception of a faster [HHb] τ in the pubertal girls during cycle ergometry. Taken together, these findings suggest that exercise intensity, but not sex, may influence training-related adaptations in O_2 utilisation, although it is important to be cognisant of the inter-study differences in training volume and commonality between training and testing modalities which may have contributed to the equivocal findings. In trained adults, enhanced O_2 utilisation has widely been attributed to an enhanced muscle oxidative capacity consequent to an increased mitochondrial volume and oxidative enzyme activity (55, 83). A similarly increased muscle oxidative capacity has been reported in trained children (36, 45) but little is known regarding the effects of training on muscle fibre type and oxidative capacities in children.

Applications of pulmonary $\dot{V}O_2$ kinetics

Overall, although less extensively investigated in children, the evidence suggests that the dynamic $\dot{V}O_2$ response is sensitive to both advantageous and deleterious influences in youth. This highlights the potential utility of $\dot{V}O_2$ kinetics in the assessment of physiological gains obtained in performance and/or public health and therapeutic environments. Indeed, in many instances, $\dot{V}O_2$ kinetics have revealed influences of exercise training or interventions not evident when conventional measures of cardiorespiratory fitness, in the form of peak $\dot{V}O_2$, are considered (80, 112). Furthermore, although the widespread reliance on peak $\dot{V}O_2$, especially within paediatric exercise science literature (3), may suggest otherwise, the applicability of this measure to daily life is questionable as it is rare that a child would reach their maximal aerobic capacity during daily activities (60). In contrast, $\dot{V}O_2$ kinetics provide an insight into the aerobic response to instantaneous changes in metabolic demand, transitions which characterise children's sporadic habitual physical activity patterns (5). In terms of clinical populations, $\dot{V}O_2$ kinetics provide a unique insight in the pathophysiological adaptations associated with the exercise intolerance that characterises many chronic conditions. For example, impairments in muscle oxidative metabolism in youth with Cystic Fibrosis have been shown to be dependent on exercise intensity (99), whilst the mechanisms of the impaired $\dot{V}O_2$ kinetics observed have been shown

to differ in adults with Emphysema and Idiopathic Pulmonary Fibrosis (79). $\dot{V}O_2$ kinetics therefore provide the potential to target therapeutic strategies to address the key exercise tolerance limiting factors.

The potential utility and applicability of $\dot{V}O_2$ kinetics is, however, currently limited by the complexities associated with its measurement and interpretation, with many fundamental questions regarding the influences of growth, maturation and external stimuli remaining to be resolved prior to its use in performance and therapeutic assessments, at least in part, due to these methodological challenges.

Methodological considerations in the assessment and interpretation of pulmonary $\dot{V}O_2$ kinetics

The somewhat limited evidence regarding $\dot{V}O_2$ kinetics in children may be attributed to a number of methodological issues which hinder their investigation in this population, first and foremost of which is the low signal-to-noise ratio in youth which is detrimental to the confidence associated with the model derived parameters, especially the τ (15). A number of factors contribute to this low signal-to-noise ratio, including a small response amplitude and generally erratic breathing pattern due to a greater variability in tidal volume and the timing of breaths than observed in adults (92). This low signal-to-noise ratio necessitates careful consideration of the exercise modality investigated, and its specificity to the training modality, if relevant, as a modality which stresses a small muscle mass will elicit a smaller response amplitude, thereby exacerbating the influence of the poor signal-to-noise ratio and potentially masking potential training-related effects. Although challenging, these limitations do not preclude the accurate characterisation of the $\dot{V}O_2$ kinetic response in children as the signal-to-noise ratio can be significantly improved by averaging repeat transitions to an identical work-rate (70). However, many studies have utilised only a single transition, reducing the confidence associated with the parameters derived.

A significant limitation of the literature is the reliance on cross-sectional studies to elucidate the influence of age, growth, maturation and training on the $\dot{V}O_2$ kinetic response. Whilst these studies have

undoubtedly significantly advanced our understanding, they are inherently limited by their inability to infer causality. Indeed, genetic predisposition, for which cross-sectional studies cannot account, is suggested to account for a considerable proportion of an individual's aerobic fitness (21, 32), potentially contributing to the variation between studies. Furthermore, the use of mixed sex cohorts, and a considerable male bias in the literature, limits potential conclusions regarding the influence of sex and its interaction with age and maturation (42).

Finally, a fundamental limitation of the studies to date is the non-invasive and, consequently, indirect methodologies that must be employed with young people. These constraints are largely responsible for the paucity of high-quality data available on children and adolescents and it is only with the relatively recent technological advances (e.g. near infrared spectroscopy) enabling indirect methodologies that significant advances in our understanding of paediatric physiology have been made. Unfortunately, even with these technological advances many questions are currently unanswerable, such as the influence of training status on muscle mitochondrial density and enzymatic profiles, leaving us to rely on a limited number of early studies.

Conclusion

The dynamic $\dot{V}O_2$ response offers a valuable and highly sensitive insight into the integrated capacity to transport and utilize O_2 to support the changes in rate of energy turnover in the contracting myocytes. Evidence remains sparse regarding the $\dot{V}O_2$ kinetic response and the factors that influence it in youth, especially during moderate and severe intensity exercise and across the maturational range. Nonetheless, the evidence suggests that age is related with a progressive slowing of the phase II τ and augmentation of the $\dot{V}O_2$ slow component, with training associated with the inverse changes in these parameters during heavy intensity exercise. The mechanistic basis for these adaptations is yet to be conclusively elucidated but may be related to the modulation of muscle phosphate controllers of oxidative phosphorylation, muscle O_2 delivery and utilisation and/or muscle fibre type recruitment strategies. Further, methodologically rigorous studies are required to fully resolve the interaction(s)

between age, sex, biological maturity and external stimuli, such as exercise training and exercise intensity, and the dynamic $\dot{V}O_2$ response at the onset and offset of exercise.

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Figure 1. Schematic illustration of the rise in muscle and pulmonary oxygen uptake at the onset of constant intensity exercise. Reproduced, with permission, from Armstrong and Barker (2)

Figure 2. Characteristic $\dot{V}O_2$ responses to the onset of exercise according to the specific exercise intensity domain. Reproduced, with permission, from Poole and Jones (89).

Figure 1.

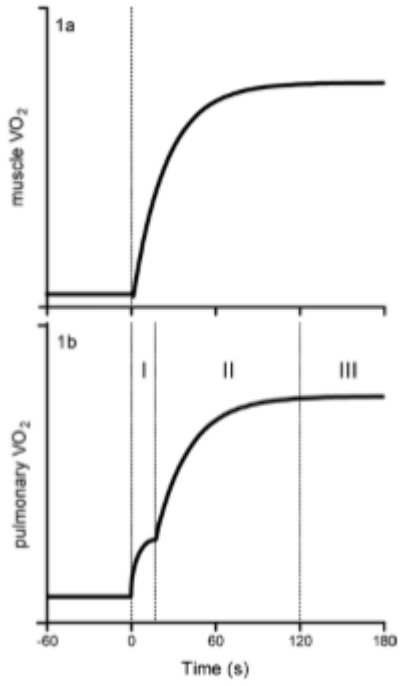
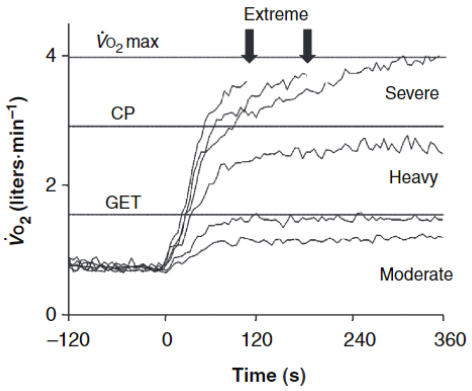


Figure 2.


Extreme
$\dot{V}O_2$ max
Severe
CP
Heavy
GET
Moderate
4
2
0
–120
0
120
240
360
$\dot{V}O_2$ (liters·min^{-1})
Time (s)