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Response



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# Reply to Korzeniewski: Muscle Bioenergetic System Properties as Common Mechanisms of V̇O2 On-Kinetics and Critical Power

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## Response

**Dear Editor-in-Chief,**

We thank Professor Korzeniewski for his letter and the opportunity to discuss further the development of concepts for an integrated understanding of the physiology that limits exercise tolerance. As we presented in the section of our review titled "$\dot{V}O_2$ kinetics and the $O_2$ deficit" (1), evidence supports that $\dot{V}O_2$ kinetics (and its fundamental phase 2 time constant, $\tau\dot{V}O_2$) are a consequence of the intracellular bioenergetic system properties, dependent on variables including oxidative phosphorylation (OXPHOS) activity, each step-activation intensity (ESA), $O_2$ and metabolite concentrations. Therefore, we agree with Professor Korzeniewski's statement that $\dot{V}O_2$ kinetics are an "epiphenomenon of the kinetic properties of the system" (2) and presented it as such in our manuscript. With knowledge of this recognized hierarchy, we would like to highlight that $\dot{V}O_2$ kinetics are a far more accessible variable to "assay" these lumped system properties non-invasively. With appropriate recognition of assumptions, such as the influence of circulatory dynamics (3), pulmonary $\dot{V}O_2$ kinetics are a close proxy of muscle $\dot{V}O_2$ kinetics (4,5), providing a non-invasive window on the overall status of the muscle bioenergetics system. In our review we gathered the evidence testing the hypothesis that interventions modifying $\dot{V}O_2$ kinetics (representing muscle bioenergetic system properties) also modify CP; we believe the weight of current evidence supports this hypothesis, and is also consistent with computer simulations of the bioenergetics system, as highlighted in Professor Korzeniewski's correspondence (Table 1 in Korzeniewski & Rossiter, (6)).

The quantitative "Pi double-threshold" mechanism, discussed in our review and formalized by Korzeniewski and Rossiter (6,7) provides new insight into these complex system

behaviors. We would like to take this opportunity to emphasize (as the original authors do) that the critical [Pi] mechanism is a proxy variable in the computer simulations representing many, potentially diverse, mechanisms that initiate a loss of efficiency in contracting muscles (increased [Pi], [ADP], $[H^+]$, reactive oxygen species, $Ca^{2+}$ sensitivity, extracellular $[K^+]$; among other candidates). Despite these recognized assumptions, the critical [Pi] represents an $O_2$-deficit-related phenomenon, initiating a loss of work efficiency from which CP emerges as a property of the entire bioenergetics system. This is the new piece of the puzzle that provides a bridge from historical efforts to associate the $O_2$-deficit with exercise tolerance, to the current hypothesis that common mechanisms in the bioenergetics system determine both $\dot{V}O_2$ kinetics and CP. We attempted to summarize this in our conclusion where we stated that fast $\dot{V}O_2$ kinetics are associated with improved metabolic stability, lesser metabolite accumulation and greater CP. Expanding on the general causal chain during rest-to-work transitions, as outlined in Professor Korzeniewski's letter, ATP breakdown at the cross-bridge leads to accumulation of Pi and ADP that interacts with the instantaneous OXPHOS activity to cause an increase in $\dot{V}O_2$. Iteratively, this then mediates how much further Pi and ADP will increase; these interactions will determine both $\dot{V}O_2$ kinetics and CP. In the trained state, adapted bioenergetics system variables, such as, but not limited to, greater OXPHOS activity and ESA result in faster $\tau\dot{V}O_2$ and an increase in CP consequent to these system adaptations allowing improved metabolic stability; hence the title of our review "Bioenergetic Mechanisms *Linking* $\dot{V}O_2$ Kinetics and Exercise Tolerance". Future investigations to test these hypotheses with experimental studies *in vivo* will undoubtedly lead to a more complete and unified understanding of the mechanisms that determine exercise intolerance.

## REFERENCES


1. Goulding RP, Rossiter HB, Marwood S, Ferguson C. Bioenergetic Mechanisms Linking $\dot{V}O_2$ Kinetics and Exercise Tolerance. Exercise and Sport Sciences Reviews. 2021 Oct;49(4):274–83. [PubMed: 34547760]
2. Korzeniewski B. $\dot{V}$O2 on-kinetics-critical power relationship: correlation but not direct causal link. Exercise and Sport Sciences Reviews.
3. Benson AP, Grassi B, Rossiter HB. A validated model of oxygen uptake and circulatory dynamic interactions at exercise onset in humans. Journal of Applied Physiology. 2013 Sep 1;115(5):743–55. [PubMed: 23766506]
4. Grassi B, Poole DC, Richardson RS, Knight DR, Erickson BK, Wagner PD. Muscle $O_2$ uptake kinetics in humans: implications for metabolic control. J Appl Physiol. 1996 Mar;80(3):988–98. [PubMed: 8964765]
5. Krustrup P, Jones AM, Wilkerson DP, Calbet J a. L, Bangsbo J. Muscular and pulmonary $O_2$ uptake kinetics during moderate- and high-intensity sub-maximal knee-extensor exercise in humans. J Physiol (Lond). 2009 Apr 15;587(Pt 8):1843–56. [PubMed: 19255119]
6. Korzeniewski B, Rossiter HB. Factors determining training-induced changes in $\dot{V}$O2max, critical power and $\dot{V}O_2$ on-kinetics in skeletal muscle. J Appl Physiol. 2021 Feb;130(2):498–507. [PubMed: 33211591]
7. Korzeniewski B, Rossiter HB. Exceeding a "critical" muscle Pi: implications for $\dot{V}$O2 and metabolite slow components, muscle fatigue and the power-duration relationship. Eur J Appl Physiol. 2020 Jul; 120(7):1609–1619. [PubMed: 32435984]