Control of $\dot{V}O_2$ Kinetics: Not a Settled Issue

Dear Editor-in-Chief,

The article "MRS evidence of adequate O_2 supply in human skeletal muscle at the onset of exercise" (7) concluded that metabolic inertia—not O_2 supply—is the major factor controlling the kinetics of $\dot{V}O_2$. This concept was supported by a delay in the increase in the deoxygenated myoglobin (deoxy-Mb) signal and similar rates of on-transient deoxy-Mb and phosphocreatine (PCr) kinetics; Richardson et al. (7) used a novel approach ([^{1}H]magnetic resonance spectroscopy) to assess deoxy-Mb and thus O_2 extraction. We were encouraged that the new technique for measuring "intramyocellular deoxygenation" responses during exercise on-transients confirmed previous measures of the time delay (TD) and time course profile of microvascular deoxygenation from our laboratory (1–3,5), using the simpler and more accessible tool of near-infrared spectroscopy. These comparative data were, however, not referenced. Nevertheless, in relation to the conclusions of the study, there are concepts that merit discussion.

First, we believe that the interpretation might be affected by fitting strategies. For example, the PCr fit was constrained to go through the onset of exercise (fixed TD) to avoid the model fit projecting into pre-exercise time. Importantly, this TD is not physiological; by forcing the fit through the onset of exercise, the quality of this model would decrease and the time constant (τ) would be artificially reduced. Additionally, the deoxy-Mb signal is very noisy (small signal-to-noise ratio; Fig. 2); thus, these model parameter estimates are tenuous. Furthermore, we disagree with the use of the model-fit TD to determine the duration of deoxy-Mb TD; we believe that this TD should be calculated from the actual physiological increase in the signal, as presented for near-infrared spectroscopy–derived deoxygenated hemoglobin response (1–3). Finally, the myoglobin τ value should be calculated based on a fitting window beginning from the end of TD; as is, the model fit includes data points that do not belong to the monoexponential increase in deoxy-Mb, and this will likely lengthen the myoglobin τ value. Thus, there might be underestimation of τPCr and overestimation of τdeoxy-Mb [see Fig. 2 in Richardson et al. (7)], affecting the conclusion that the adjustment of deoxy-Mb was similar to PCr kinetics.

We agree that O_2 supply to the active tissues does not determine the rate of adjustment of $\dot{V}O_2$ kinetics during the early phase of exercise. Indeed, recently, we reformulated the "tipping point" concept (4) that Richardson et al. referred to (6) and proposed that when $\tau\dot{V}O_2$ is less than or equal to approximately 20 s, $\dot{V}O_2$ adjustment is O_2-independent (intracellularly controlled). However, our work indicated that when the $\dot{V}O_2$ kinetics response is slower than approximately 20 s, O_2 provision to tissues is critical in determining the adjustment of oxidative phosphorylation (4). Although we do not expect Richardson et al. (7) to share our views, we believe that their conclusion that metabolic inertia—not O_2 supply—is the major limitation to the full on-transient $\dot{V}O_2$ kinetics is an overstatement and cannot be supported by the data presented. Thus, we would hope that Richardson et al. (7) could accept that alternative views on the topic should have been at least acknowledged.

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REFERENCES

1. Murias JM, Kowalchuk JM, Paterson DH. Speeding of $\dot{V}O_2$ kinetics in response to endurance-training in older and young women. *Eur J Appl Physiol*. 2010;111(2):235–43.
2. Murias JM, Kowalchuk JM, Paterson DH. Speeding of $\dot{V}O_2$ kinetics with endurance training in old and young men is associated with improved matching of local O_2 delivery to muscle O_2 utilization. *J Appl Physiol*. 2010;108(4):913–22.
3. Murias JM, Spencer MD, Kowalchuk JM, Paterson DH. Muscle deoxygenation to $\dot{V}O_2$ relationship differs in young subjects with varying $\tau\dot{V}O_2$. *Eur J Appl Physiol*. 2011;111(12):3107–18.
4. Murias JM, Spencer MD, Paterson DH. The critical role of O_2 provision in the dynamic adjustment of oxidative phosphorylation. *Exerc Sport Sci Rev*. 2014;42(1):4–11.
5. Murias JM, Spencer MD, Pogliaghi S, Paterson DH. Noninvasive estimation of microvascular O_2 provision during exercise on-transients in healthy young males. *Am J Physiol Regul Integr Comp Physiol*. 2012;303(8):R815–23.
6. Poole DC, Barstow TJ, McDonough P, Jones AM. Control of oxygen uptake during exercise. *Med Sci Sports Exerc*. 2008;40(3):462–74.
7. Richardson RS, Wary C, Walter Wray D, et al. MRS evidence of adequate O_2 supply in human skeletal muscle at the onset of exercise. *Med Sci Sports Exerc*. 2015;47(11):2299–307.