Interpreting the phosphocreatine time constant in aerobically exercising skeletal muscle

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TO THE EDITOR: Francescato et al. (1) contrast the lack of interindividual correlation between the phosphocreatine (PCr) time constant ($\tau_{PCr}$) and the ADP concentration ([ADP]) change from rest to steady state ($\Delta[ADP]_S$) during moderate aerobic exercise with the fact that “...ADP concentration is commonly thought to be one of the main feedback signals controlling mitochondrial respiration” (1), a view supported by observations that initial postexercise PCr resynthesis rate [=mitochondrial ATP synthesis rate ($J_P$) at end exercise (5)] has a roughly hyperbolic (Michaelis-Menten) relationship to $[ADP]$ (2, 3). The general idea is that $J_P/J_{P,\text{MAX}}$ is some property that response kinetics are independent of perturbation (1); however, variation in $J_{P,\text{MAX}}$ would make $\Delta[PCr]$ and $\tau_{PCr}$ covary [which they do not (1)] without obliging rejection of the linear model, e.g., in favor of feedforward mechanisms (1).

Francescato et al. (1) also conclude, from the correlation between $\tau_{PCr}$ and $[PCr]_R$, that PCr concentration is “one of the main controllers of oxidative phosphorylation” (1). But consider three sources of variation in $[PCr]_R$: if only $J_{P,\text{MAX}}$ varied, adjustments in $[ADP]_R$ would yield a negative $\tau_{PCr}$-$[PCr]_R$ correlation (1), opposite to that observed (1); variation in $J_{D,R}$ (separate from variation in $J_{D,S}$) would affect $[ADP]_R$ and thus $[PCr]_R$, not $\tau_{PCr}$; but if $[TCr]$ varied, $[PCr]_R$ would vary proportionately to maintain $[ADP]_R$, giving a positive $\tau_{PCr}$-$[PCr]_R$ correlation with $\Delta[PCr]/\Delta[PCr]_R \approx 1$, close to that observed (1).

In summary, without information on variation in ATP turnover and $[TCr]$, the noncorrelation of $\tau_{PCr}$ with $\Delta[ADP]_S$ and $\Delta[PCr]_S$ (1) (and as $pH_S \approx pH_R$, each noncorrelation implies the other) has no definite implications for ADP-feedback or -feedforward mechanisms (1). Possible causes of $\tau_{PCr}$-$[PCr]_R$ correlation (1) include interindividual variation in $[TCr]$.

REFERENCES


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Type I fibers have higher $J_{P,\text{MAX}}$ but lower $[PCr]_R$ than type II (1), but model explanation must await data on differences in, e.g., $[TCr]$ and consensus on $f(X)$ (2, 3, 7).