The classic potentiation of exercise ventilatory response by increased dead space in humans is more than short-term modulation

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TO THE EDITOR: Wood et al. (9) report that end-tidal PCO2 (PETCO2) in young men increases with increased external dead space (DS) at rest and equally so during moderate exercise, such that the slope of the resultant ventilation (VE)-metabolic CO2 production (VCO2) relationship is potentiated. The authors call this potentiation effect in humans “short-term modulation.” Apart from this change of nomenclature and substitution of PETCO2 for arterial PCO2 (PaCO2), these observations are little different from earlier reports of similar effects based on careful alveolar PCO2 (PACO2) (8) or PaCO2 measurements in humans (2). The authors (9) submit that PaCO2, in exercise could be estimated from PETCO2 via the Jones equation (1) but “decided not to present [those] values” after all since they believe that “measuring the change in PETCO2 from rest to exercise was sufficiently accurate.”

This argument is flawed. Not only was the Jones equation not meant for studies with sizable external DS, but the latter might result in significant increases in PaCO2-PACO2 difference (6), which could be highly variable during exercise. In any event, there seems little to gain by reverting to PETCO2 in lieu of thorough PACO2 or PaCO2 measurements in characterizing the classic potentiation of the VE-VCO2 relationship that has been long established with even wider range of external DS and age range in humans (2, 8).

Methodological issues aside, the authors (9) contend that these classic studies either “did not seek to address” the notion of short-term modulation or “rejected [it] and instead suggested that within-breath oscillations of PaCO2 may constitute a signal during exercise, which is heightened by dead space, resulting in increased ventilatory drive. . . . In addition, Poon postulated that his observations could be explained by an optimization theory of the respiratory controller.” The authors are correct about the significance of the optimization theory (4) in predicting the effect of external DS on exercise ventilatory response but are mistaken about the relevance of PaCO2 oscillation as “ventilatory drive” and the relevance of the peripheral chemoreceptors in its mediation. In Ref. 2 it is stressed that “PaCO2 oscillation may be involved in a more complex mode of neural information processing within the respiratory controller than merely acting as a feedback or feedforward signal” and that “peripheral chemoreceptors mediation, although important, is not obligatory for this behavior.”

The presumed short-term modulation ascribed by the authors to spinal mechanisms (9) cannot explain the distinct potentiation of VE-VCO2 by airway CO2 and by external DS and the age dependence of such potentiation effects reported in Ref. 2, an even greater potentiation of VE-VCO2 by physiological DS as seen in congestive heart failure (3), or increases in VE-PaCO2 slope and corresponding ventilatory load compensation when the hypercapnia is induced by external DS instead of airway CO2 (7), all of which are accurately predicted by the optimization theory (4). Presently, it is unclear whether such a general optimization behavior in humans involves spinal mechanisms. For a latest update of the optimization theory and its general predictability of these and other respiratory effects and its possible underlying mechanisms, the authors are referred to Ref. 5.

REFERENCES

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