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 P_{CO_2} (PET_{CO_2}) 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 (V̇E)-metabolic CO_{2} production (V̇C_{O_2}) relationship is potentiated. The authors call this potentiation effect in humans “short-term modulation.” Apart from this change of nomenclature and substitution of PET_{CO_2} for arterial P_{CO_2} (P_{ACO_2}), these observations are little different from earlier reports of similar effects based on careful alveolar P_{CO_2} (P_{ACO_2}) (8) or P_{ACO_2} measurements in humans (2). The authors (9) submit that P_{ACO_2} in exercise could be estimated from PET_{CO_2} via the Jones equation (1) but “decided not to present [those] values” after all since they believe that “measuring the change in PET_{CO_2} 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 P_{ACO_2}-P_{ACO_2} difference (6), which could be highly variable during exercise. In any event, there seems little to gain by reverting to PET_{CO_2} in lieu of thorough PACO_{2} or PaCO_{2} measurements in characterizing the classic potentiation of the V̇E-V̇C_{O_2} 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 P_{ACO_2} 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 PACO_{2} oscillation as “ventilatory drive” and the relevance of the peripheral chemoreceptors in its mediation. In Ref. 2 it is stressed that “P_{ACO_2} 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 V̇E-V̇C_{O_2} by airway CO_{2} and by external DS and the age dependence of such potentiation effects reported in Ref. 2, an even greater potentiation of V̇E-V̇C_{O_2} by physiological DS as seen in congestive heart failure (3), or increases in V̇E-P_{ACO_2} slope and corresponding ventilatory load compensation when the hypercapnia is induced by external DS instead of airway CO_{2} (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