The Last Word: Point:Counterpoint authors respond to commentaries on “Supraspinal locomotor centers do/do not contribute significantly to the hyperpnea of dynamic exercise in humans”

To the Editor: The reactions to the debate on the role of supraspinal (hypothalamic/mesencephalic) locomotor centers (SLC) in controlling ventilation during exercise show that this question is far from futile (3). Many respiratory physiologists and neurophysiologists are still accepting the challenge of the resolution of the control of exercise hyperpnea, even after a long history of research on the topic!

I would like to respond to the various points addressed by Dr. Eldridge in his letter (3).

First, a vigorous marshalling of evidence in defense of a point of logic is a welcome and essential component of a properly scientific exchange; a jibe (“antidiluvian”) is not.

Second, the major problem with a model purely based on a locomotor control is that it can not account for the slow development of the normal minute ventilation ($V_e$) response to exercise ($V_e$ time constant is 60 s; i.e., it takes 3 min for $V_e$ to reach a steady state). Eldridge argued in most of his reviews that by adding a short-term potentiation (STP) component (2), one can explain such slow dynamics. The flaw here is that the kinetics of such STP phenomenon during stimulation of the respiratory neurons is much too fast (on-time constant of few seconds; see Ref. 2 for review) to account for the $V_e$ on-transient kinetics during exercise. In addition, where has such a phenomenon been shown to operate during the on-transient of exercise in humans?

Third, the use of voluntary hyperventilation is entirely spurious. What is the rational for using the observation that $V_e$ may remain slightly elevated (for 10–20 s!) after a voluntary hyperventilation (9) to explain the response to exercise? Does Eldridge assume that recovery from voluntary hyperventilation involves the same control system as exercise?

Fourth, the contribution of arterial plasma concentration ([K$^+$]$_a$) as a significant stimulus to breathe during exercise has been disproved by the very same group who promoted this idea (7). How? By preventing a rise in [K$^+$]$_a$ during exercise using β-blockers (7, 8). The result was the same $V_e$ response despite totally different [K$^+$]$_a$ (see also Ref. 10). If so, why is Eldridge using such a mechanism as a valid hypothesis to account for $V_e$ phase II and III? Does he mean that this idea was proposed after the “deluge”?

Fifth, “what about the circulatory response?” wonders Eldridge. Mechanisms controlling both the cardiovascular and the respiratory systems according to the level of metabolic rate have been proposed (see Refs. 5 and 6 for review). Whether new ideas will hold with time depends only on the refutation from other experiments and not on dogma.

Sixth, it is difficult to see the results of Asmussen et al. (1) or Goodwin et al. (4) as proof for a role of SLC. First, the fact that contractions of partially “curarized” muscles produce an exaggerated response does not imply that the same mechanism is regulating breathing during unimpeeded exercise (1). Second, what central command are we referring to here? Certainly not SLC when dealing with static contractions (4)! Many supramedullar structures can affect $V_e$, but whether SLC is a fundamental controller of breathing during exercise is a totally different matter.

Finally, Eldridge is far too dismissive of the implications of the considerable body of evidence suggesting a metabolic-coupled mechanism for at least part of the hyperpnea; mere correlation, he asserts! As if correlation were not an important first step toward a properly mechanistic design: it provides a signpost to the resolution—it is not an impediment. But failing to consider its logical consequences is!

REFERENCES


Philippe Haouzi
Laboratoire de Physiologie
Faculté de Médecine et CHU de Nancy
Nancy, France
e-mail: p.haouzi@chu-nancy.fr