To the Editor: This is regarding the recent Point:Counterpoint series on supraspinal mechanisms involved in exercise hyperpnea (5). I will not repeat the arguments of the “Point” article for the central command mechanism, but suggest that a perusal of several extensive reviews might be rewarding [Eldridge and Waldrop (3), Waldrop and Iwamoto (“Point” Ref. 24)].

Houazi (5) bases his criticism of central command on what he calls “spectacular” findings in humans and sheep during oscillatory changes of work rates where a good correlation was found between gas exchange and ventilation. In this regard, the comments of Dempsey et al. (2) are pertinent: that such studies yield only correlative data, which clearly fail to separate cause and effect. Houazi nevertheless dismisses the central command mechanism as well as other probable neural and chemical [K+] signals (3), and ends up contending that ventilation is constrained to follow information related to gas exchange rate, albeit “through unclear mechanisms,” to “neglect” other information and that CO2 homeostasis is the main “goal” of the ventilatory response to exercise. This kind of approach is both teleological and antidiluvian.

Other points follow. First, Houazi avoids discussion of cardiovascular responses. These are fast and probably related to central command. Does he believe that these are also due to the mysterious CO2 mechanism he postulates?

Second, he says no real attempt to test the CC mechanism in humans has been made. What about the study with static exercise [Goodwin et al. (“Point” Ref. 24)] that demonstrated the CC mechanism for respiratory and circulatory changes and the study by Asmussen et al. (1) in curarized humans?

Third, although he dismisses short-term potentiation (STP), which has, by the way, been demonstrated in humans (4), it could affect interpretation of his sheep studies. TP’s onset is relatively fast, but it has a decay time constant of 40–50 s (“Counterpoint” Ref. 25) so this afterdischarge would still be present during the shorter periods of work oscillation in his studies and would affect ventilation.

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To the Editor: Studies of cardiorespiratory responses during exercise must identify the impulse for exercise, whether peripheral or central. If from the center, we study afferent modulation of central command; if from the periphery (“treadmill on”), we study how afferent signals trigger locomotory action and cardiorespiratory responses. Any “corticated” preparation may have a central motor/behavioral/emotional response to “treadmill on.” Experiments performed with motor imagery show that no signal from the periphery is necessary for...
the complex cardiorespiratory responses to perceived exercise (3). Documenting that the stimulation of specific central areas responsible for inducing locomotion also might adjust breathing and circulation to anticipated muscular effort is therefore very interesting. Unanswered questions remain. How is central command organized (2)? How does it affect motor outputs (1), including subpopulations of pattern generators (see Ref. 5 and this author’s other papers on locomotion)? How does training affect central regulation (3)? How are afferent signals processed, by creating an error signal with the descending command or by integrating exercise effects in “the plethysmometric” signal (4), directly affecting cardiorespiratory reflexes? What is the time factor of studied responses?

Regarding Haouzi’s paper (4), Fig. 1, three segments with different time scales recalibrated to the same lengths, is misleading: in a 30-s interval of high frequency walking for a longer cycle, the maximal effort lasts longer than during the same interval for the shorter cycle. Ventilation is higher with longer effort (for \( T = 5 \) min). Also, ventilatory response is delayed by a comparable time in all presented runs.

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To the Editor: The current controversy (4) regarding the contribution of supraspinal locomotor centers to human exercise appears to center on different dynamic components of exercise hyperpnea. According to the neurohumoral theory of Dejours (2), the fast (neural) component occurs within a few seconds and the slow (humoral) component requires minutes to develop. Dejours recognized that the “humoral” component could involve peripheral mechanoreceptive sensors (3). Haouzi (4) in using sinusoidally changing treadmill speed of up to 1 cpm frequency can only measure the slow component (1), whereas Waldrop and Iwamoto’s (4) stimulation methods focus on the fast component. Sinusoidal forcing at 1 cpm is incapable of resolving the fast “neural” component, which is most likely connected with central command and supraspinal locomotor centers. However, the slow component still represents about one-half of the overall response (2).

Species differences cloud interpretation, inasmuch as both groups based their conclusions on different animal experiments (sheep and cats). Another methodological issue that can be mentioned is whether sinusoidal locomotor forcing at different frequencies can be considered the same in view of different input locomotor power levels (frequency \( \times \) cycle kinetic energy change). The cycle kinetic energy change is the same if treadmill speed excursions are kept the same, but power varies with sinusoidal frequency. At least in the steady state, metabolic rate correlates better with locomotor power rather than just speed.

Both central command and peripheral mechanoreceptors seem to play equally important roles in human exercise hyperpnea.

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The definitive answer is still unclear. Dr. Haouzi's advice to keep searching for the “primary mechanisms regulating breathing in exercise.” I strongly agree with Dr. Haouzi's advice to keep searching for and fine tuning of cardiorespiratory function in exercise. In the end, both feedback and central command are involved in the regulation of which regulates cardiorespiratory function in response to any stressor, be it peripheral or central in origin. In the end, both feedback and central command are involved in the regulation and fine tuning of cardiorespiratory function in exercise. I strongly agree with Dr. Haouzi’s advice to keep searching for the “primary mechanisms regulating breathing in exercise.” The definitive answer is still unclear.

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pneumonia of muscular exercise—before moving on to other pursuits! This comment appears to be as relevant today as it was over 35 years ago (3).

My own (transient) foray into this field was facilitated by the generosity of my colleague Joel Cooper, who was using an awake sheep preparation to study the effects of a veno-venous, extracorporeal membrane lung on platelet function; part of the research program that led to the first successful human lung transplant (1). The Cooper lab and sheep preparation were put at my disposal for a series of studies in which we compared (in the same animal) the ventilatory response to moderate steady-state exercise (treadmill walking) and the response to venous infusions of CO₂ at rest (through the membrane lung).

Somewhat to our surprise, we found that the relationship between ventilation and the rate of CO₂ production (at the lungs of the sheep) could be described by a single linear function, regardless of whether CO₂ production was increased by exercise, venous infusions of CO₂, or combinations of both procedures (2). We therefore concluded that, in this intact muscles, exercise is terminated. Breathlessness is distinct from tolerate the exertional discomfort with the limb or respiratory function, regardless of whether CO₂ production was increased lungs of the sheep) could be described by a single linear steady-state exercise.

fication of neural mechanisms in exercise hyperpnea in other settings, they suggest that there is no need to invoke obligatory nonmetabolic stimuli to account for the ventilatory response to steady-state exercise.

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To the Editor: Mathematical equations, introduced by the pioneers of respiratory physiology, were exploited in this debate (2). However, understanding requires a broader point of view.

Neurophysiologists, biochemists, and respiratory physiologists view limitation from different points of view. Any explanation should be satisfactory to all. That limitation is ultimately a neural event, with activation and termination arising within the brain, is a logical and defensible explanation.

A central motor command activates the motor units in the spinal cord, leading to depolarization, calcium release, and muscle shortening. The motor command, accompanied by a sense of exertional discomfort intensifies with power and time (effort = k⋅power².0⋅time⁰.3). When the subject can no longer tolerate the exertional discomfort with the limb or respiratory muscles, exercise is terminated. Breathlessness is distinct from exertional effort arising with respiratory failure (hypercapnia and hypoxemia) when the capacity of the lungs to exchange gas is exceeded. Breathlessness is easily demonstrated by holding one’s breath. The responsiveness of the muscle to the motor command depends on its physiological support. Hence, more effort is required to generate and sustain power with reduced perfusion, hypoxemia, acidemia, carbohydrate depletion, and/or any breakdown in the physicochemical equilibrium.

The Henderson’s equation ([H⁺] = 24 Pco₂/[HCO₃⁻]) is a valid description of a physicochemical relationship. However, the late Peter Steward (1) elegantly demonstrated that understanding acid-base control requires consideration of the several other equally valid physicochemical relationships obeyed. These same limitations apply to the equations used in this debate.

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