Invited Editorial on “Effects of chest wall vibration on breathlessness during hypercapnic ventilatory response”

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Over the past 20-30 years, substantial progress has been made in our understanding of dyspnea. We have come to the realization that dyspnea encompasses a number of distinct sensations (16) and that a diverse array of receptors in the chest wall, lungs, airways, and central nervous system may influence the quality and intensity of an individual’s respiratory sensation. In this issue, Edo and colleagues (5) add to our growing body of knowledge with their finding that, in healthy volunteers, vibration applied to the inspiratory intercostal muscles during inspiration and to the expiratory intercostal muscles during expiration (so called “in-phase vibration”) decreases the breathlessness induced by hypercapnia and an inspiratory resistive load. Their results are consistent with previous studies, which have found that, depending on the site and timing of the vibratory stimulus, chest wall vibration decreases breathlessness induced in both normal subjects (9) and in patients with chronic lung disease (15).

By what mechanism does something as seemingly unrelated to respiration as vibration reduce breathlessness? The study by Edo et al. (5) provides no direct evidence in this regard, but a number of animal studies provide the basis for reasonable conjecture. Two experimental findings are particularly relevant: 1) vibration is a potent stimulus to skeletal muscle receptors, especially muscle spindles (12), and 2) intercostal muscle vibration reduces medullary inspiratory activity (3, 4). This makes it tempting to invoke stimulation of muscle spindles as the cause of the reduced dyspnea associated with chest wall vibration, but intercostal tendon organs and costovertebral joint receptors might also play a role (3, 4). Another possibility considered by the authors is that, by contributing to the activation of the inspiratory muscles, the tonic vibration reflex, a spinal segmental reflex elicited by intercostal muscle vibration, decreases the central motor command, thereby decreasing the sense of respiratory effort and dyspnea. However, since vibration has previously been shown to affect the sensation of breathlessness in settings where the sense of effort likely plays little role (7), the tonic vibration reflex is probably not the mechanism by which vibration exerts its effects on breathlessness.

The study by Edo and colleagues (5) also illustrates the many parallels between respiratory control and respiratory sensation. Although much remains unknown about the fundamental mechanisms that give rise to the respiratory rhythm, we do know that the final “shape” of the respiratory output is modulated by the net effect of multiple afferent inputs. These afferent inputs can be viewed from the perspective of both the general stimulus (e.g., a change in inspiratory flow rate) and the specific receptors (e.g., irritant receptors) that respond to the stimulus. Some of the afferent signals affecting central inspiratory activity (CIA), such as those arising in muscle spindles and pulmonary stretch receptors, are inhibitory, whereas others, such as those arising from the chemoreceptors, pulmonary irritant receptors, and C fibers, exert an excitatory effect. Although in humans it is generally difficult, if not impossible, to isolate a stimulus to a specific respiratory receptor or to know which receptor (s) has been stimulated under a given set of conditions, the effect of a stimulus on dyspnea can be predicted on the basis of its effects on CIA. Thus stimulation of pulmonary stretch receptors (10) or, as the study by Edo et al. (5) suggests, intercostal muscle spindles reduces dyspnea, whereas stimulation of the peripheral and central chemoreceptors by hypercapnia (2) and/or hypoxia increases breathlessness, as does stimulation of irritant receptors (13, 17) and, possibly, C fibers (11).

The study by Edo et al. (5) demonstrates another characteristic shared by the central neural mechanisms governing respiratory control and respiratory sensation: the effects of many stimuli vary with the phase of the respiratory cycle during which they are applied. For example, in an animal study by Gandevia and McCloskey (6), inspiratory chest wall (sternal) vibration caused a decrease in tidal volume, but the same vibratory stimulus applied during expiration had no effect on tidal volume. A similar pattern is seen with the effects of chest wall vibration on dyspnea: in-phase vibration reduces dyspnea (9, 15), whereas out-of-phase vibration causes dyspnea to increase (7, 15).

The discussion up until now leads to an obvious question: is breathlessness simply the perception of CIA? If so, that would, in fact, provide a long-sought-after unifying mechanism of dyspnea. Unfortunately, two factors make it particularly difficult to answer that question. First, we have no direct “window” on CIA in humans; we must instead draw inferences about CIA from outputs that we can measure directly, such as ventilation, occlusion pressure at 0.1 s, diaphragm...
EMG, etc. Second, the pathways and interactions between cortical and brain stem respiratory centers are largely obscure. For example, what happens to CIA when volition "overrides" the brain stem and generates a level of ventilation above or below that dictated by chemical drive?

With those caveats in mind, we can at least ask whether the respiratory system behaves in a manner consistent with the hypothesis that dyspnea arises from the perception of CIA. In addition to the parallels already mentioned above, it appears that the magnitude of dyspnea correlates with the level of reflexly determined ventilation, regardless of the specific ventilatory stimulus (8). An extreme example of this can be seen in children with congenital central hypoventilation syndrome. These children, who lack a ventilatory response to hypercapnia, experience no sensation of air hunger while breathing CO₂ (14). When Banzett (1) examined the dynamic-response characteristics of CO₂-induced air hunger in normal subjects, he found that the time course of the air-hunger response to hypercapnia approximates the time course of the ventilatory response to CO₂. Thus the quantitative and temporal characteristics of dyspnea conform fairly well to what we would expect if dyspnea were to arise from the perception of CIA. However, the "CIA hypothesis" falls short when it comes to explaining differences in the quality of dyspnea. If dyspnea were solely a function of the magnitude of CIA, all breathlessness would feel the same. Yet, that is clearly not the case. Both normal subjects and patients describe a variety of qualitatively different sensations. For example, exercise, hypercapnia, and resistive loads all feel different; the sensation of methacholine-induced bronchoconstriction differs from that of an external load (13). If the perception of CIA is to maintain a tenable role as the principal mechanism underlying the sensation(s) of breathlessness, the hypothesis must be modified to account for qualitative aspects of breathlessness. Further studies may help unravel such details.

REFERENCES