Carotid Bodies and Expiratory Muscle Recruitment*
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We have reported previously (FASEB J 1989; 3:A401) that specific carotid body stimulation/inhibition tended to recruit/derecruit expiratory muscles in the same direction, and with similar time course, as the diaphragm in unanesthetized dogs (N = 5). One limitation of that study was the presence of pulmonary vagoafferent traffic that could have had an effect on expiratory muscle recruitment independent of the direct carotid body effects. To address this question, we blocked the pulmonary stretch receptor afferent traffic by bilateral cooling of exteriorized (skin loops) cervical vagi in 3 awake, tracheotomized dogs. Excitatory (NaCN, 3-5 breaths N2) and inhibitory (dopamine, 3-5 breaths O2) stimuli of the carotid bodies during vagal blockade produced effects similar to those seen in non-blocked dogs; recruitment/derecruitment of expiratory muscles (triangularis sterni, transversus abdominis) was in the same direction and had the same time course as changes in the crural diaphragm.

We conclude that pulmonary stretch receptor afferents are not required for inspiratory or expiratory muscle recruitment/derecruitment in response to carotid body stimuli.

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Role of Inspiratory Muscle Dysfunction in Chronic Hypercapnia*
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Hypercapnia can be caused by increased CO2 production (VCO2), decreased minute ventilation (VE) (central or peripheral), or abnormal ventilation-perfusion relationship. We explored the possible role of respiratory muscle dysfunction as a cause of chronic hypercapnia in chronic obstructive pulmonary disease (COPD). We surveyed 269 clinically stable COPD patients, of whom 55 had a PaCO2 ≥ 45 mm Hg. Lung resistance (Rl), dynamic lung compliance (Ct), and maximal inspiratory pressure (MIP) at FRC were measured via an esophageal balloon catheter. Forced expiration (FEV1), VE, fractional CO2 concentration of mixed expired gas, and blood gases at rest were also measured.

Hypercapnic and normocapnic patients were found to have a similar VCO2, VE, tidal volume (VT), and frequency of breathing. The Vn/Vt was higher in hypercapnic subjects (.57 ± .08 vs 50 ± .08, p < .001). A significant relationship was found between PaCO2 and Rl (r = .53) and between PaCO2 and FEV1 and Ct. (r = .48 and r = .42, respectively). Rl was also related to the mean intrathoracic inspiratory pressure swing (r = .82) and a multiple regression analysis showed a strong interaction between Rl and MIP-1 (F = 20.6) in predicting PaCO2. Indeed, all 13 patients with Rl/MIP ≥ .33 were hypercapnic. This subgroup had lower Vt than patients with Rl/MIP < .33 (8.8 ± 1.9 vs 10.3 ± 2.6 L/min, p < .05). The slope of the PaCO2-Rl/MIP relationship was higher in a subgroup of obese patients (weight > 120% predicted) vs a subgroup of nonobese patients (p < .01). Logistic regression analysis demonstrated that the probability of being hypercapnic was greater than 50% in a nonobese patient when RL/MIP exceeded 0.27 and in an obese patient when RL/MIP was greater than 0.20.

Our data showed that hypercapnia occurred when the inspiratory muscles were required to develop a tidal pressure greater than one-third of the MIP. It is well documented that, although these patients can reduce their PaCO2 by increasing the Vt, this strategy induces fatigue. These data suggest that inspiratory muscle loading may trigger a reflex hypoventilation to prevent inspiratory muscle fatigue and failure.

Hypoxic Exposure and Activation of the After-Discharge Mechanism*
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It has been shown that after voluntary hyperventilation normal people do not develop a significant ventilatory depression, despite the low PaCO2, a phenomenon attributed to activation of a brain-stem mechanism (after-discharge). After-discharge is one of the factors that promotes ventilatory stability. At present, in humans, after-discharge is evaluated with voluntary hyperventilation, which requires subjects’ cooperation. It is not known if physiologic stimuli, such as hypoxia, can activate the after-discharge mechanism in humans. To test this, in 9 young adults, breath-by-breath ventilation (V) was measured during and immediately after a brief period (35 s) of acute hypoxia (end-tidal O2 concentration [ETCO2] 55 mm Hg). Hypoxia was terminated by switching to 100% O2 with a small dead space (ETO2 of first posthypoxic breath > 100 mm Hg). Furthermore, in order to see if sustained hypoxia interferes with after-discharge, in 14 subjects hypoxia was sustained for 25 min and breath-by-breath V was measured as FIO2 was increased to 100%. At the end of brief hypoxia, turning off the carotid bodies by hypoxia resulted in a gradual decline in V toward baseline over 10-20 s without an undershoot, despite the lower ETCO2, indicating activation of the after-discharge mechanism by brief hypoxia. On the contrary, when hypoxia followed sustained (25-min) hypoxia, and despite normocapnic conditions, there was an abrupt drop in V, lasting for several breaths, to values that were well below the hypoxic levels (range 81%-20%).

It follows that sustained hypoxia interferes with the development of after-discharge. This effect destabilizes ventilation and may contribute to the periodic breathing of high altitude. Brief exposure to hypoxia might be a useful test for after-discharge evaluation without requiring the subject’s cooperation.

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