The Effect of Hyperoxia on Muscle Sympathetic Nerve Activity: A Systematic Review and Meta-Analysis

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BACKGROUND

- Changes in arterial oxygen content cause reflexive changes in peripheral chemoreflex signaling originating at the carotid bodies (Figure 1).
- Hypoxia, or low oxygen, causes an increase in muscle sympathetic nerve activity (MSNA; Figure 2).
- It remains less clear whether hyperoxia, or high oxygen, causes an opposite decrease in MSNA. It is also unclear the extent to which the response to hyperoxia differs between apparently healthy individuals and those with chronic diseases.

We sought to investigate if:

- Hyperoxia causes a decrease in MSNA in healthy individuals and those with chronic cardio-metabolic diseases.

METHODS

- Systematic review of electronic databases.
- Population: humans of all ages.
- Exposure: hyperoxia (fraction inspired oxygen >21%) or hyperbaria (ambient pressure >1atm).
- Comparison: normoxia vs. hyperoxia or hyperbaria.
- Outcomes: measures of muscle sympathetic nerve activity. Secondary outcomes included heart rate, blood pressure, and minute ventilation.
- We calculated mean differences (MD) and 95% confidence intervals (CI) for all outcome variables.

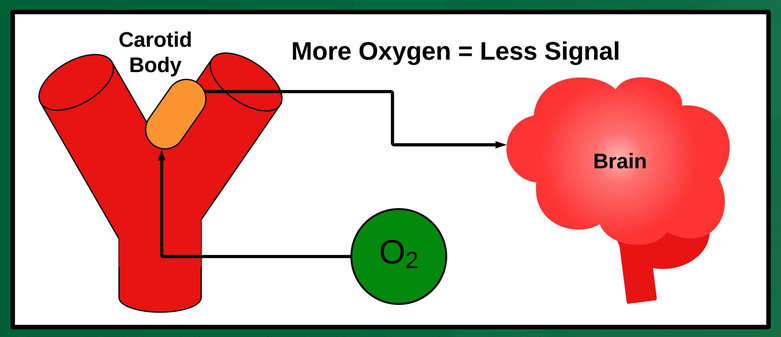

Figure 1. Peripheral chemoreflex signaling depends on arterial oxygen content.

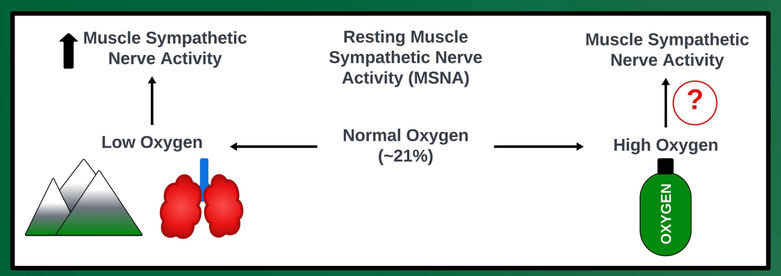

Figure 2. Decreases in oxygen, via exposure to high altitude or chronic hypoxemia caused by a chronic disease, elicit a consistent increase in muscle sympathetic nerve activity (left). It remains less clear how increases in oxygen, from supplemental oxygen administration, affect muscle sympathetic nerve activity (right).

RESULTS

- Forty-nine studies met our inclusion criteria.
- Thirty-two studies reported data on apparently healthy individuals.
- Twenty-three studies reported data on individuals with chronic diseases.

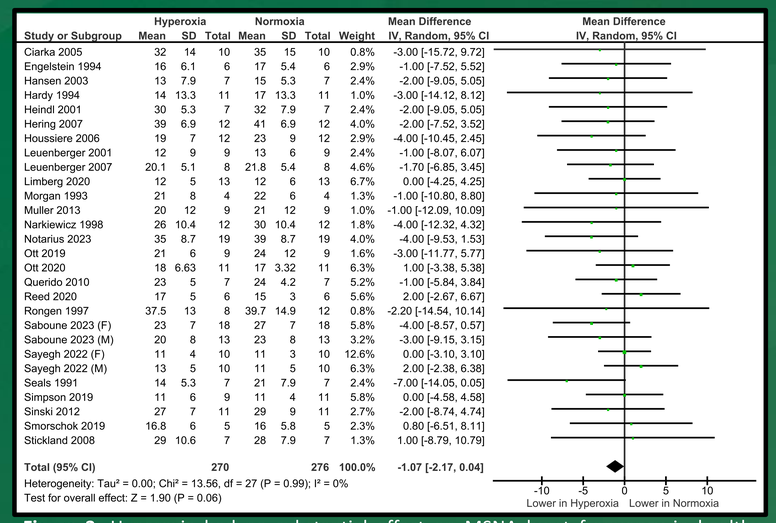

Figure 3. Hyperoxia had no substantial effect on MSNA burst frequency in healthy humans (MD = -1.07 bursts/min; 95% CI = -2.17, 0.04 bursts/min; P = 0.06). Analyses were conducted with a random-effects model. df, degrees of freedom; IV, inverse variance; F, female; M, male.

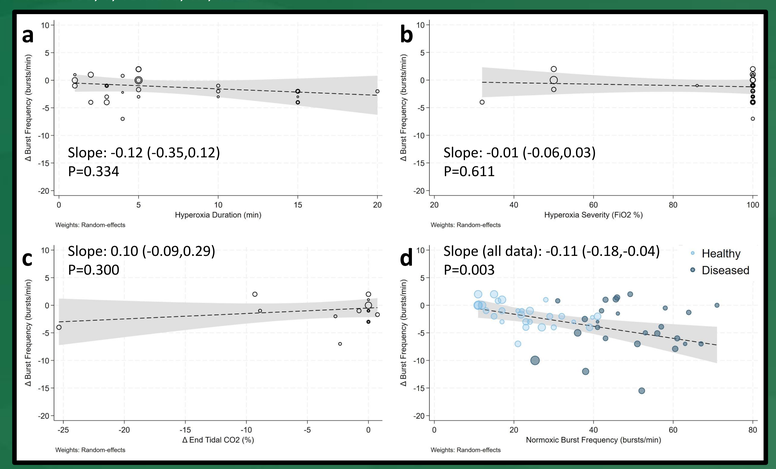

Figure 4. None of hyperoxia duration (A), severity of hyperoxia (B), or the percent change in end-tidal partial pressure of carbon dioxide from normoxia to hyperoxia (C) affected sympathetic burst frequency in healthy individuals. Conversely, in all individuals (i.e., healthy and diseases), we found an inverse relationship between normoxic burst frequency and change in burst frequency with hyperoxia (D). Circles represent individual studies, with the size indicating the proportional weighting of the data. Slopes are presented as means (95% confidence interval).

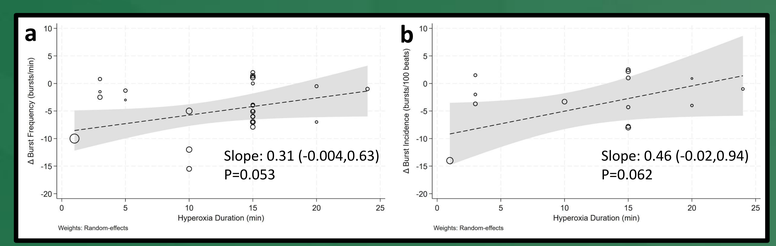

Figure 5. Relationships between sympathetic burst frequency (A) and burst incidence (B) vs. hyperoxia duration in humans with chronic diseases. Circles represent individual studies, with the size indicating the proportional weighting of the data. Slopes are presented as means (95% confidence interval).

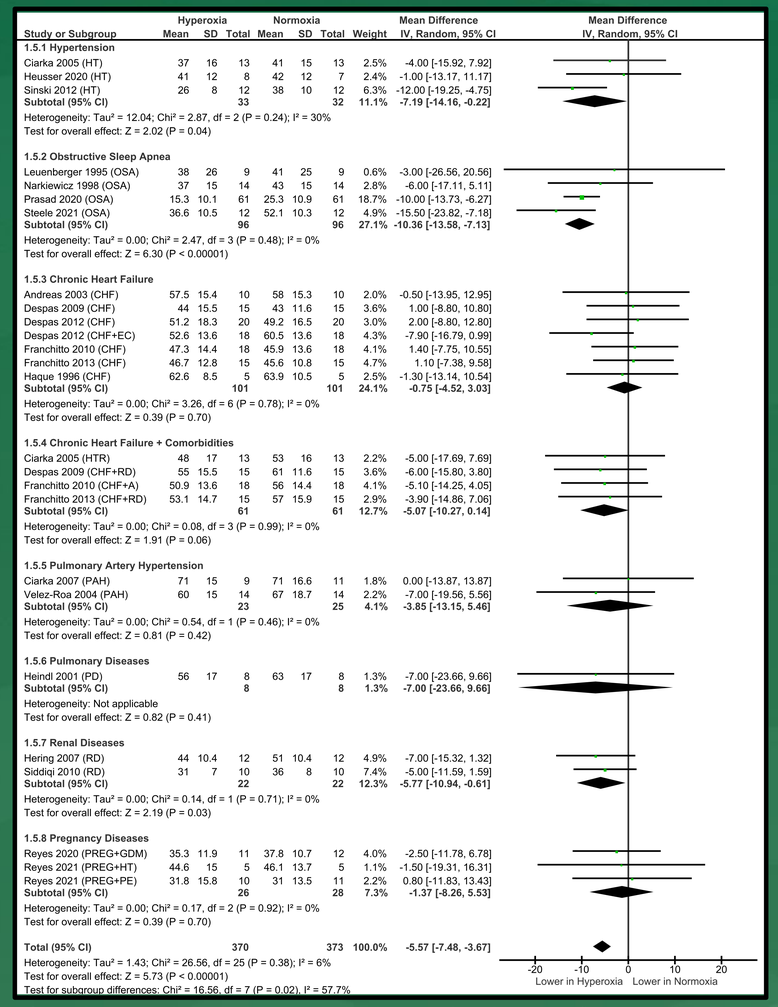

Figure 6. Hyperoxia caused a substantial decrease in MSNA burst frequency in humans with chronic diseases (MD = -5.57 bursts/min; 95% CI = -7.48, -3.67 bursts/min; P < 0.001). Analyses were conducted with a random-effects model. df, degrees of freedom; IV, inverse variance; HT, hypertension; OSA, obstructive sleep apnea; CHF, chronic heart failure; EC, elevated chemoreflex; HTR, heart transplant recipients; RD, renal diseases; A, anemia; PAH, pulmonary artery hypertension; PD, pulmonary diseases; PREG, pregnant; GDM, gestational diabetes mellitus; PE, pre-eclampsia.

INTERPRETATIONS

- We clarified the assumption that hyperoxia decreases MSNA in healthy individuals; they are either "as low as they can go" or other mechanisms negate the effect of oxygen on the peripheral chemoreceptors.
- Acute hyperoxia ameliorates elevated sympathetic activity in individuals with chronic diseases, suggesting that these pathological conditions exhibit altered chemoreflex functioning.

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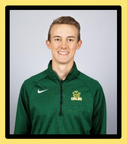

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