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## **Human hypoxic ventilatory response with blood dopamine content under intermittent hypoxic training.**

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Adaptation to intermittent hypoxia can enhance a hypoxic ventilatory response (HVR) in healthy humans. Naturally occurring oscillations in blood dopamine (DA) level may modulate these responses. We have measured ventilatory response to hypoxia relative to blood DA concentration and its precursor DOPA before and after a 2-week course of intermittent hypoxic training (IHT). Eighteen healthy male subjects (mean 22.8±2.1 years old) participated in the study. HVRs to isocapnic, progressive, hypoxic rebreathing were recorded and analyzed using piecewise linear approximation. Rebreathing lasted for 5-6 min until inspired O<sub>2</sub> reached 8 to 7%. IHT consisted of three identical daily rebreathing sessions separated by 5-min breaks for 14 consecutive days. Before and after the 2-week course of IHT, blood was sampled from the antecubital vein to measure DA and DOPA content. The investigation associated pretraining high blood DA and DOPA values with low HVR ( $r = -0.66$  and  $-0.75$ , respectively), elevated tidal volume ( $r = 0.58$  and  $0.37$ ) and vital capacity ( $r = 0.69$  and  $0.58$ ), and reduced respiratory frequency ( $r = -0.89$  and  $-0.82$ ). IHT produced no significant change in ventilatory responses to mild hypoxic challenge (P<sub>et</sub>O<sub>2</sub> from 110 to 70-80 mm Hg; 1 mm Hg = 133.3 Pa) but elicited a 96% increase in ventilatory response to severe hypoxia (from 70-80 to 45 mm Hg). Changes in HVRs were not accompanied by statistically significant shifts in blood DA content (24% change), although a twofold increase in DOPA concentration was observed. Individual subject's changes in DA and DOPA content were not correlated with HVR changes when these two parameters were evaluated in relation to the IHT. We hypothesize that DA flowing to the carotid body through the blood may provoke DA autoreceptor-mediated inhibition of endogenous DA synthesis-release, as shown in our baseline data.

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