

Interaction of CBF reactivity to hypoxia and to hypercapnia

Zachary M Smith¹, Ethan Li¹, and David J Dubowitz¹

¹Center for Functional MRI, University of California San Diego, La Jolla, California, United States

Introduction: CBF and pulmonary ventilation both increase in response to isolated hypercapnia or hypoxia. When these stimuli are combined the CBF and ventilatory responses are further augmented. To separate out the individual reactivity to hypercapnia and hypoxia, we measured CBF during isolated isocapnic hypoxia, and iso-oxic hypercapnia. To assess the interaction, we also made measurements during combined hypoxia and hypercapnia. To study the impact of acclimatization to prolonged hypoxia on the cerebral reactivity to O₂ and CO₂, measurements were repeated after 7 days of sustained hypoxia. Results were compared with similar measurements of pulmonary ventilation reactivity.

Methods: CBF responses were measured using PICORE QUIPSS2 ASL technique (TE=9.1ms, TR=2.5s, TI₁=700ms, TI₂=1500ms, 6 mm slices, 3.5 mins). CBF measurements were corrected for physiological noise and the effect of O₂ desaturation on T₁ of blood. O₂ saturation was continuously monitored with a MRI-compatible pulse oximeter calibrated against an arterial blood sample. Ventilation was measured using a pneumotach while in the scanner.

A partial rebreathing circuit allowed independent control of ETCO₂ and SaO₂. Measurements were made during:

- (1) 100% vs. 90% SaO₂ with ETCO₂ clamped to normocapnic levels
- (2) 100% SaO₂ with normocapnia vs. +5 torr ETCO₂ hypercapnia
- (3) 90% SaO₂ with normocapnia vs. +5 torr ETCO₂ hypercapnia.

17 healthy subjects participated, measured at baseline during normoxia and after 7-days sustained hypoxia (3,800m alt, mean SaO₂ 87%) (age 29.5 ± 9 yrs, 9F, 8M).

Results: Table 1 shows the CBF and ventilation reactivity to isolated hypoxia (ΔSaO₂) and isolated hypercapnia (ΔPaCO₂). After acclimatization to sustained hypoxia, CBF showed diminished (~0.5 fold) hypoxia sensitivity, whereas ventilation showed increased (~3 fold) hypoxia sensitivity. Reactivity to CO₂ increased for both CBF (~30%) and ventilation (~20%) following acclimatization.

For combined hypercapnic and hypoxic stimuli, both CBF and ventilation reactivity increased at baseline and after 7-days acclimatization to hypoxia. At baseline, the CBF and ventilatory responses are different: The CBF response to hypercapnia shows an additive increase with hypoxia (p<0.05), but no gain change in CO₂ sensitivity (slope unchanged). However, ventilation shows a multiplicative effect with an increase in resting CBF (p<0.001) as well as a gain change in CO₂ sensitivity (slope changed) (p<0.001). Following 7 days hypoxic acclimatization, CBF and ventilation behave more similarly. Both show a multiplicative effect of combined hypoxia and hypercapnia with increased resting CBF or ventilation (p<0.05) and increased gain to CO₂ (slope increased) (p<0.05).

Discussion: The different responses highlight differences in CBF and ventilatory control. Ventilation sensitivity to hypoxia is via peripheral chemoreceptors primarily in the carotid bodies, and appears capable of amplification following prolonged hypoxic acclimatization. By contrast, the cerebrovascular response to hypoxia appears attenuated by prolonged hypoxic exposure. It has been shown that the ventilatory response to combined hypercapnia + hypoxia results in an amplification of the response by the peripheral chemoreceptors. For CBF reactivity, the CO₂ is believed to act locally at the arterioles themselves. The arteriolar sensor for hypoxia is less clear. At baseline this local interaction appears limited to an additive response. The mechanism underlying a switch from additive to multiplicative CO₂ + hypoxia reactivity after prolonged hypoxic acclimatization warrants further investigation.

CBF	Baseline	7-days Hypoxia
Isolated ΔSaO ₂ (ml/100ml/min/Δ%SaO ₂)	1.08±0.21	0.63±0.07**
Isolated ΔPaCO ₂ (ml/100ml/min/Δtorr CO ₂)	1.97±0.29	2.55±0.33
Ventilation	Baseline	7-days Hypoxia
Isolated ΔSaO ₂ (L/min/Δ%SaO ₂)	0.20±0.02	0.63±0.15**
Isolated ΔPaCO ₂ (L/min/Δtorr CO ₂)	1.10±0.25	1.32±0.22

Table 1: CBF and Ventilation reactivity to isolated hypoxia (ΔSaO₂) or isolated hypercapnia (ΔPaCO₂). (mean ± SE, ** P<0.05 relative to Baseline)

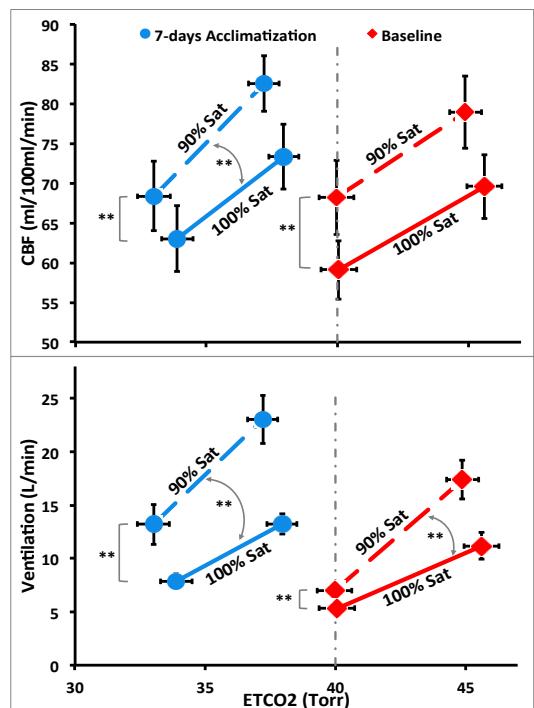


Figure 1: CBF and ventilation reactivity for CO₂ (solid line) and for combined CO₂ plus hypoxia (dashed line) at baseline and after 7-days hypoxic acclimatization, demonstrating additive and multiplicative interaction. (mean ± SE, ** P<0.05 for changes in slope or resting CBF / ventilation).

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