



Brain Glutamate and GABA: Mediation of the Physiological and Toxic Effects of Hyperbaric Oxygen

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Background:

Our previous work indicates that HBO₂ below 3 ATA inhibits sympathetic outflow and improves cardiac function through a baroreflex mechanism while HBO₂ above 3 ATA results in sympathetic overdrive and vagal withdrawal associated with oxygen seizures and lung injury.

Physiology of Moderate and Extreme Hyperbaric Oxygen

Motor behavior:
no noticeable motor disturbances

Autonomic:
parasympathetic activation

Cardiovascular:
vasoconstriction, bradycardia, cardiac output decrease

Respiration: hypopnea

Motor behavior:
local muscle twitching, tonic and clonic convulsion

Autonomic:
sympathetic overexcitation

Cardiovascular: hypertension, cerebral hyperemia, tachycardia

Respiration: hyperpnea

Hypothesis: Physiological or Toxic Effects of Moderate or Extreme HBO₂ are Attributable to Central Glutamate/GABA Imbalance.

Aim: The aim of the present study was to elucidate an implication of the glutamatergic and GABAergic systems in physiological and toxic effects of HBO₂, ultimately to find ways of preventing or mitigating CNS and pulmonary HBO₂ toxicity.

Methods:

Animals: SD rats

HBO₂: 2.5 or 5 ATA

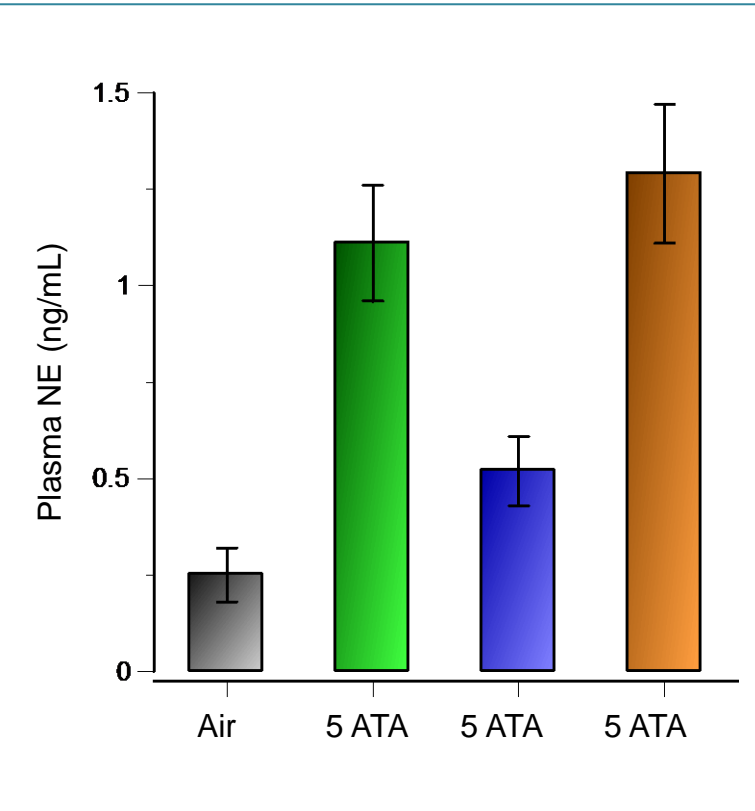
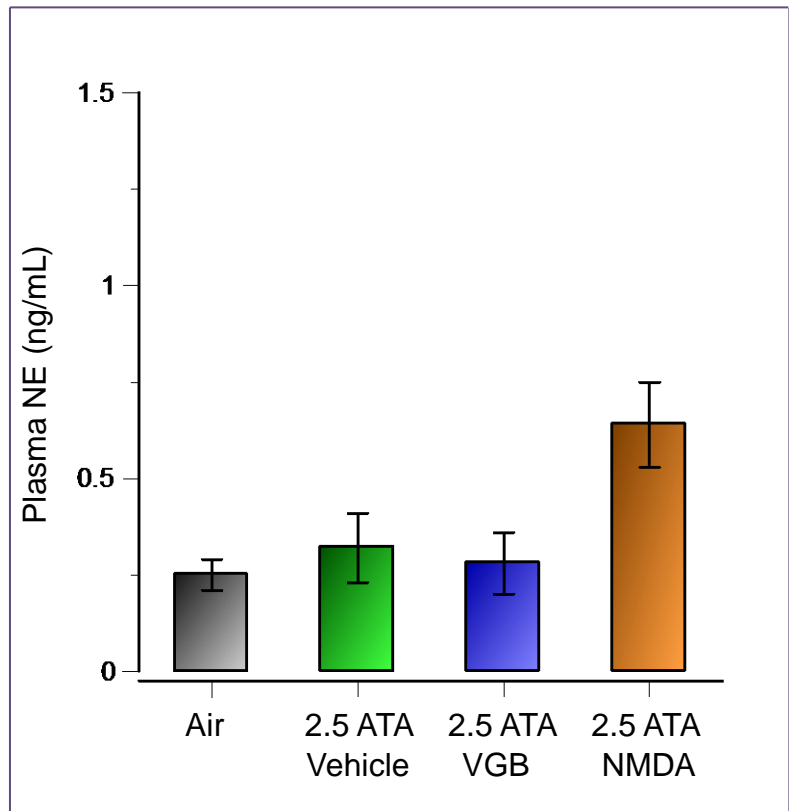
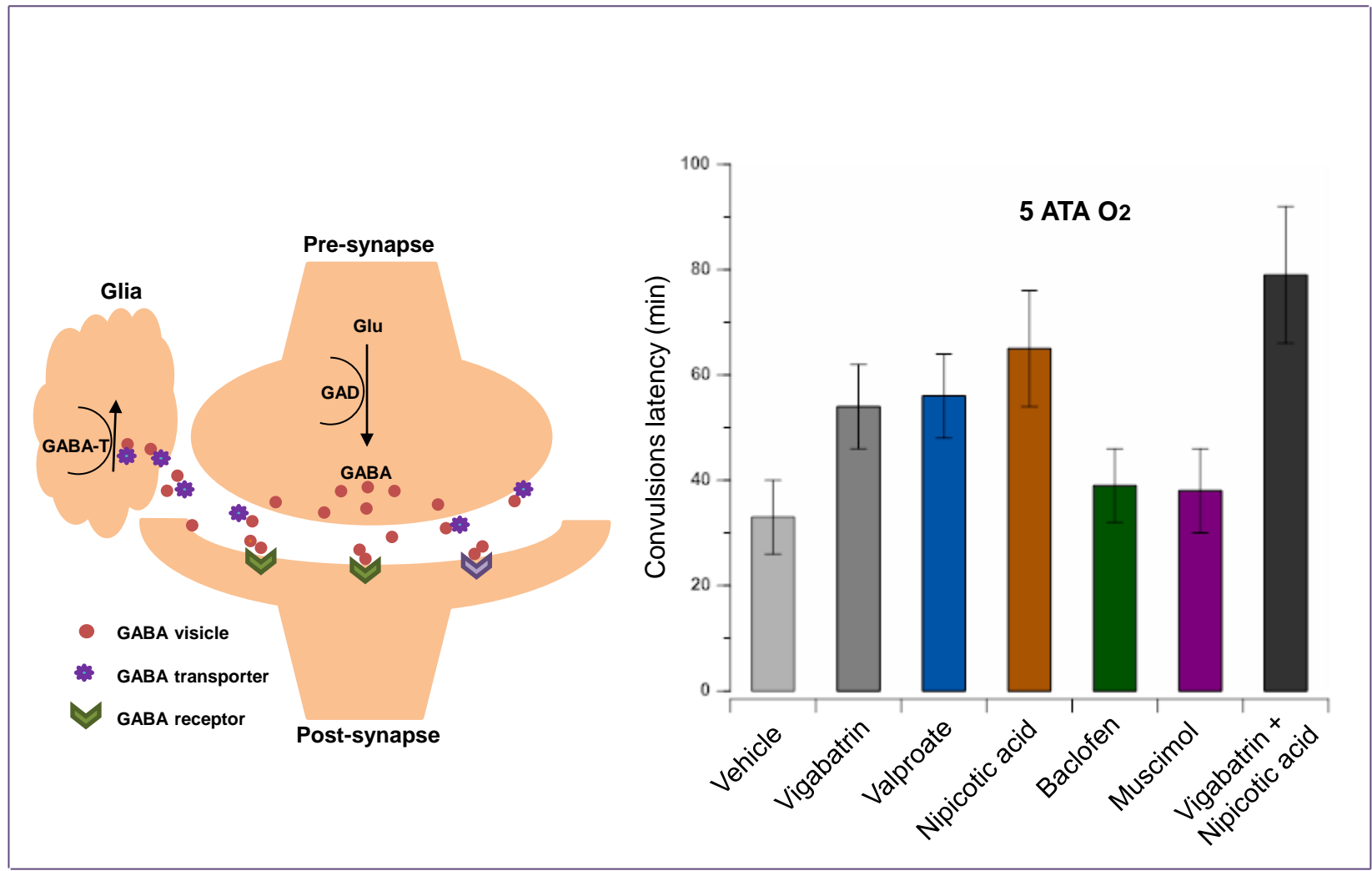
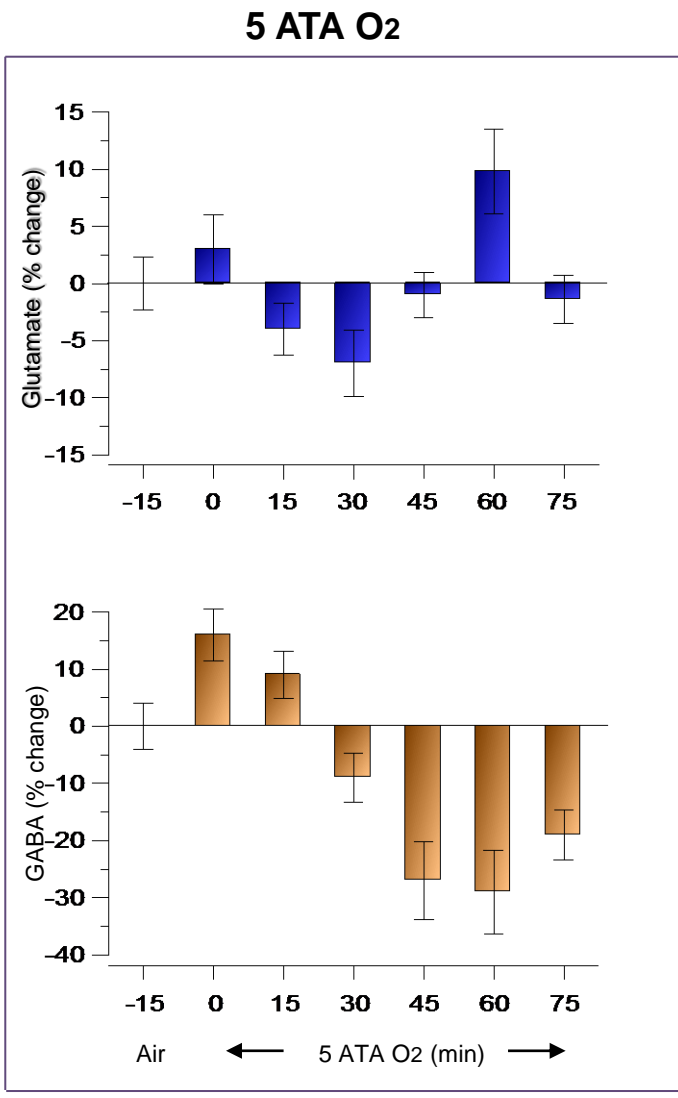
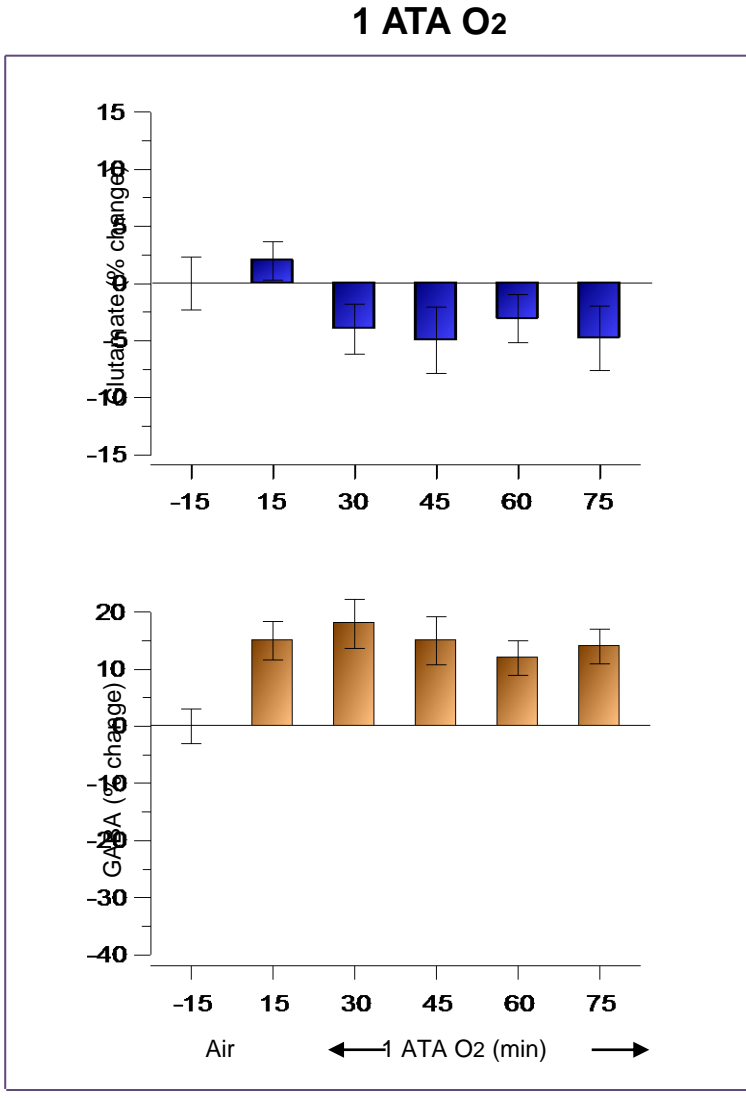
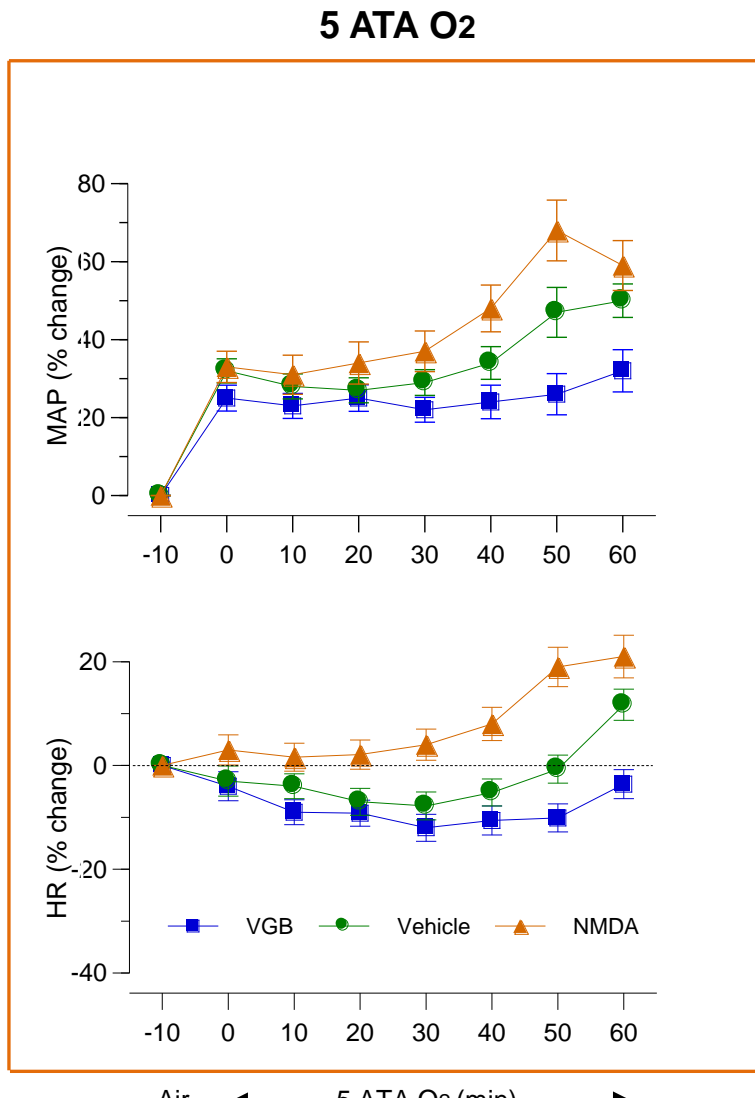
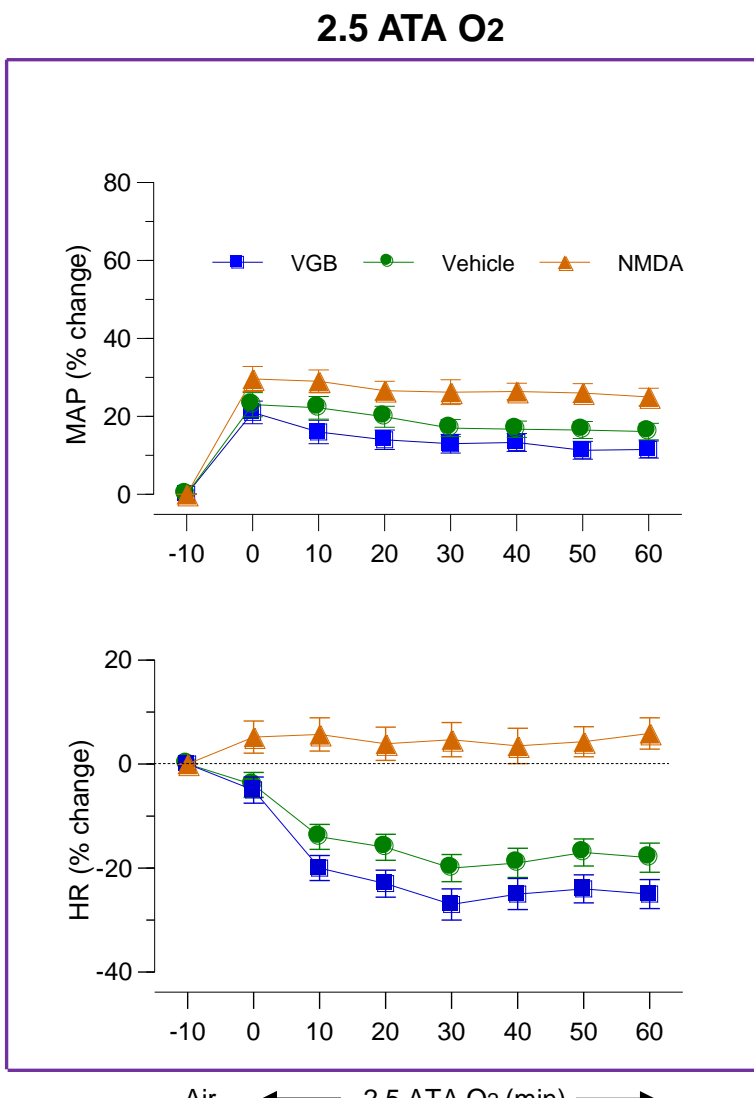
Measurements: Brain glutamate and GABA, arterial and heart ventricular pressures, cardiac output, heart rate, renal sympathetic nerve activity

Monitoring: EEG, ECG

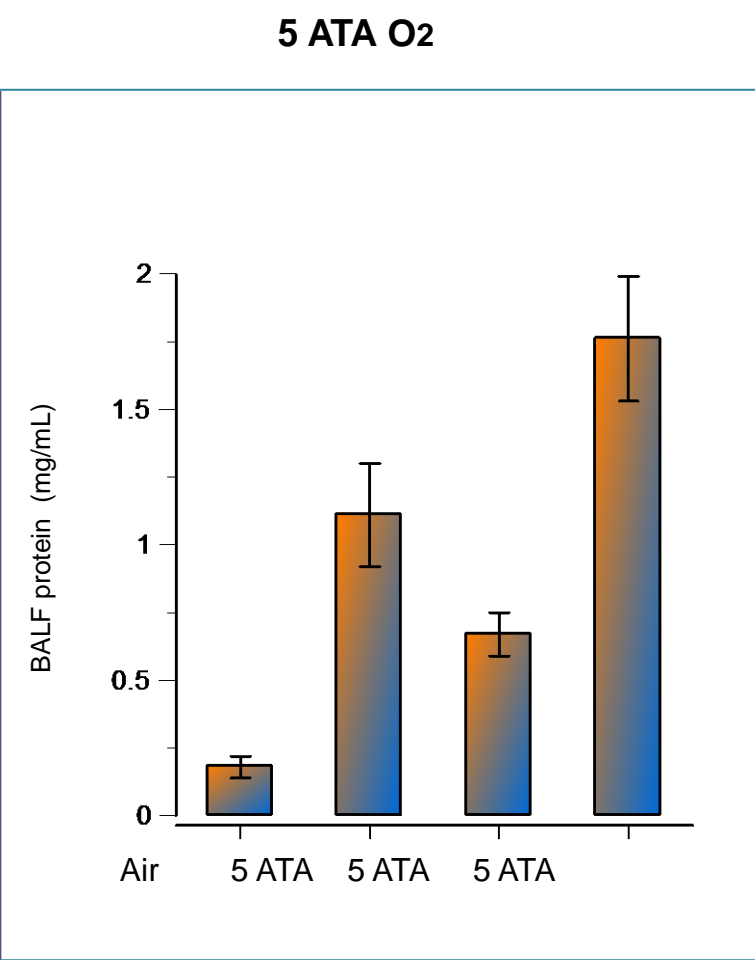
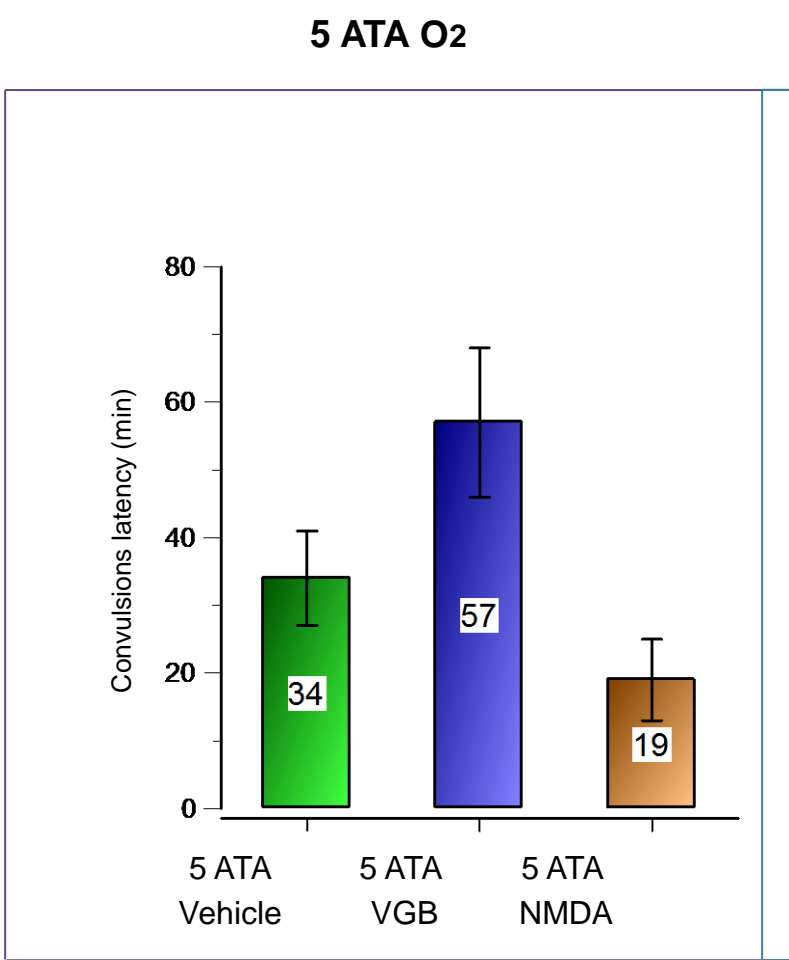
HBO₂ toxicity: EEG spikes, convulsions latency

Study approach:

Alteration of Glutamate or GABA neurotransmission by intracerebroventricular injection of Vigabatrin or NMDA

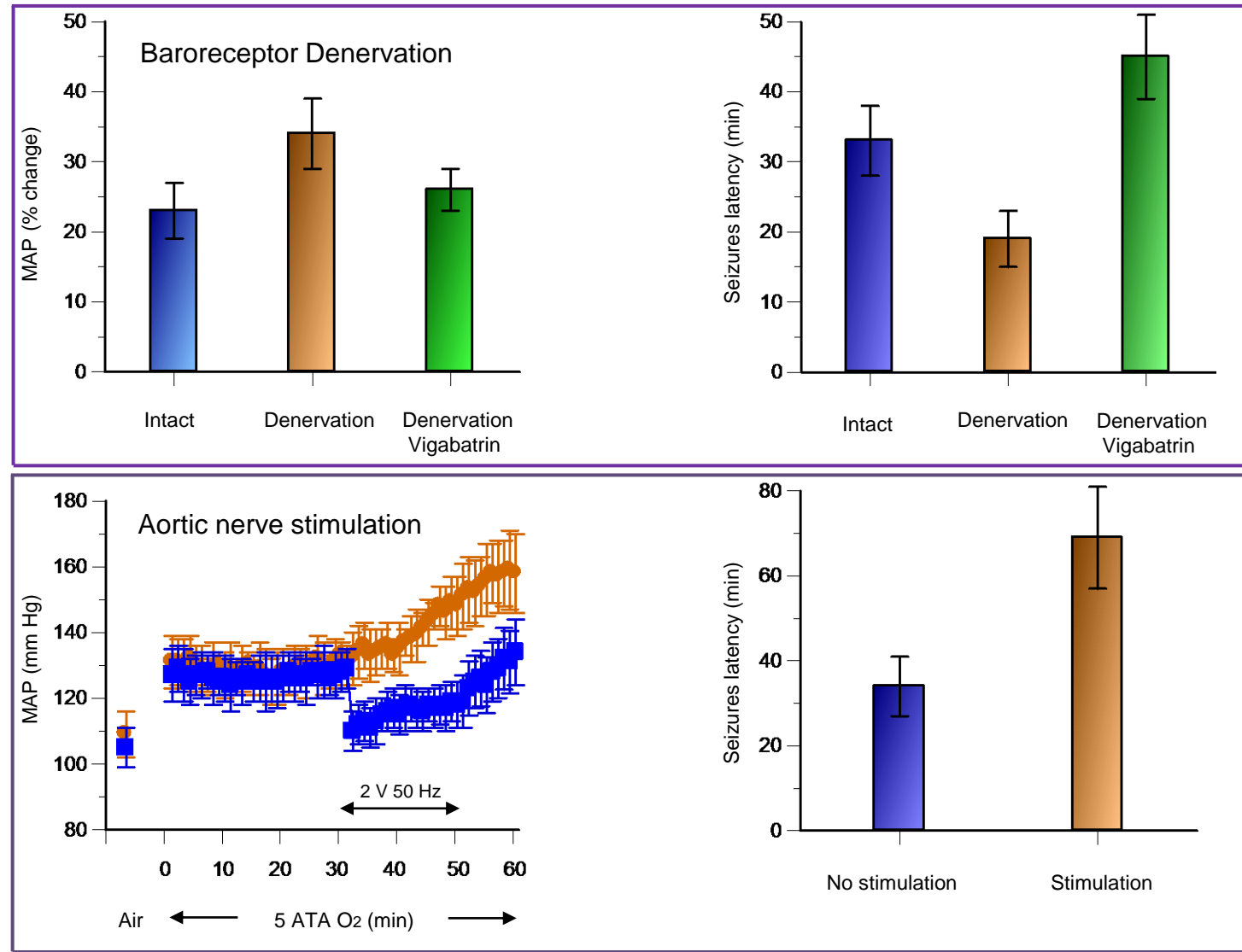


Glutamate/GABA Mediated Cardiovascular and Autonomic Responses to HBO₂



Glutamate/GABA Mediated HBO₂ Seizures and Lung Injury

Glutamate and GABA Release in Rat Striatum in Hyperoxia



GABA Mediated HBO₂ Seizures are Modulated by Baroreceptor Activity

Effects of GABA-transmission Activation on HBO₂ related Seizures

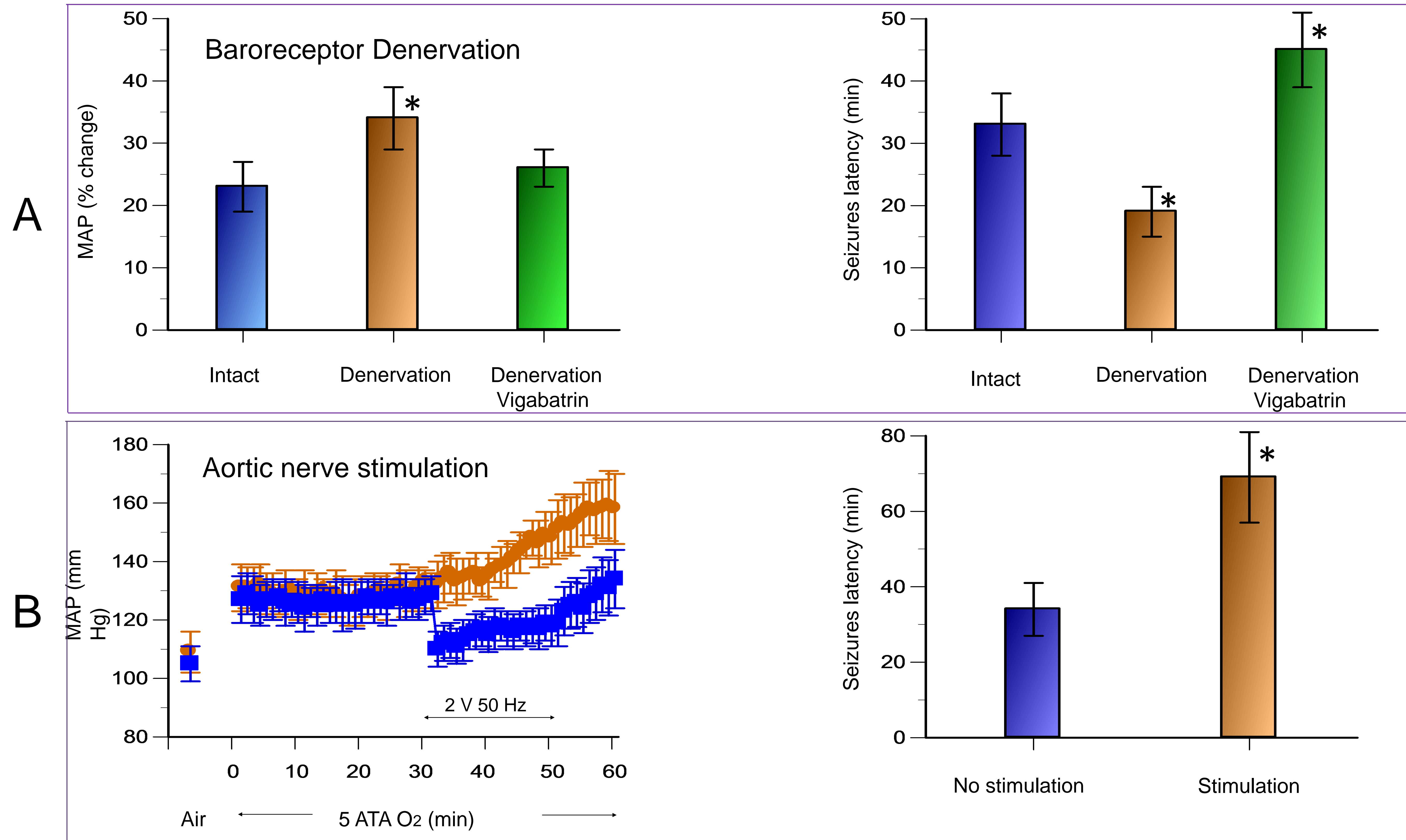
Conclusions

- Moderate HBO₂ levels (<3 ATA) inhibit efferent sympathetic drive by baroreflex-mediated elevation of GABAergic tone.
- HBO₂ above 3 ATA increases glutamatergic tone and NO production that together suppress GABA neurotransmission, triggering convulsions, peripheral sympatho-excitation and lung injury.
- Findings suggest unique pharmacological strategies for prevention of CNS and pulmonary HBO₂ toxicity.

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GABA Mediated HBO₂ Seizures are Modulated by Baroreceptor Activity



GABA Mediated HBO₂ Seizures are Modulated by Baroreceptor Activity

