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

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Physiology of Moderate and Extreme Hyperbaric Oxygen

2.5 ATA O_2 (60 min)

Motor behavior:
no noticeable motor disturbances

Autonomic:
parasympathetic activation

Cardiovascular:
vasoconstriction, bradicardia, cardiac output decrease

Respiration: **hypopnea**

5 ATA O_2 (60 min)

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 HBO_2 are attributable to central Glutamate/GABA imbalance

Methods:

Animals: **SD rats**

HBO_2 : **2.5 or 5 ATA**

Measurements:

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

Monitoring:

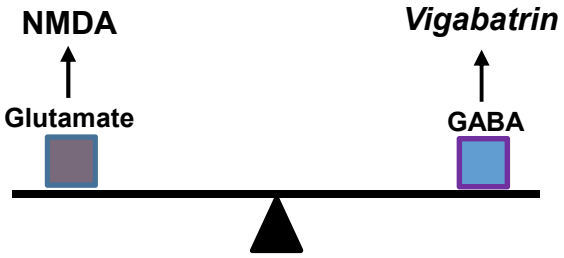
EEG, ECG

HBO_2 toxicity:

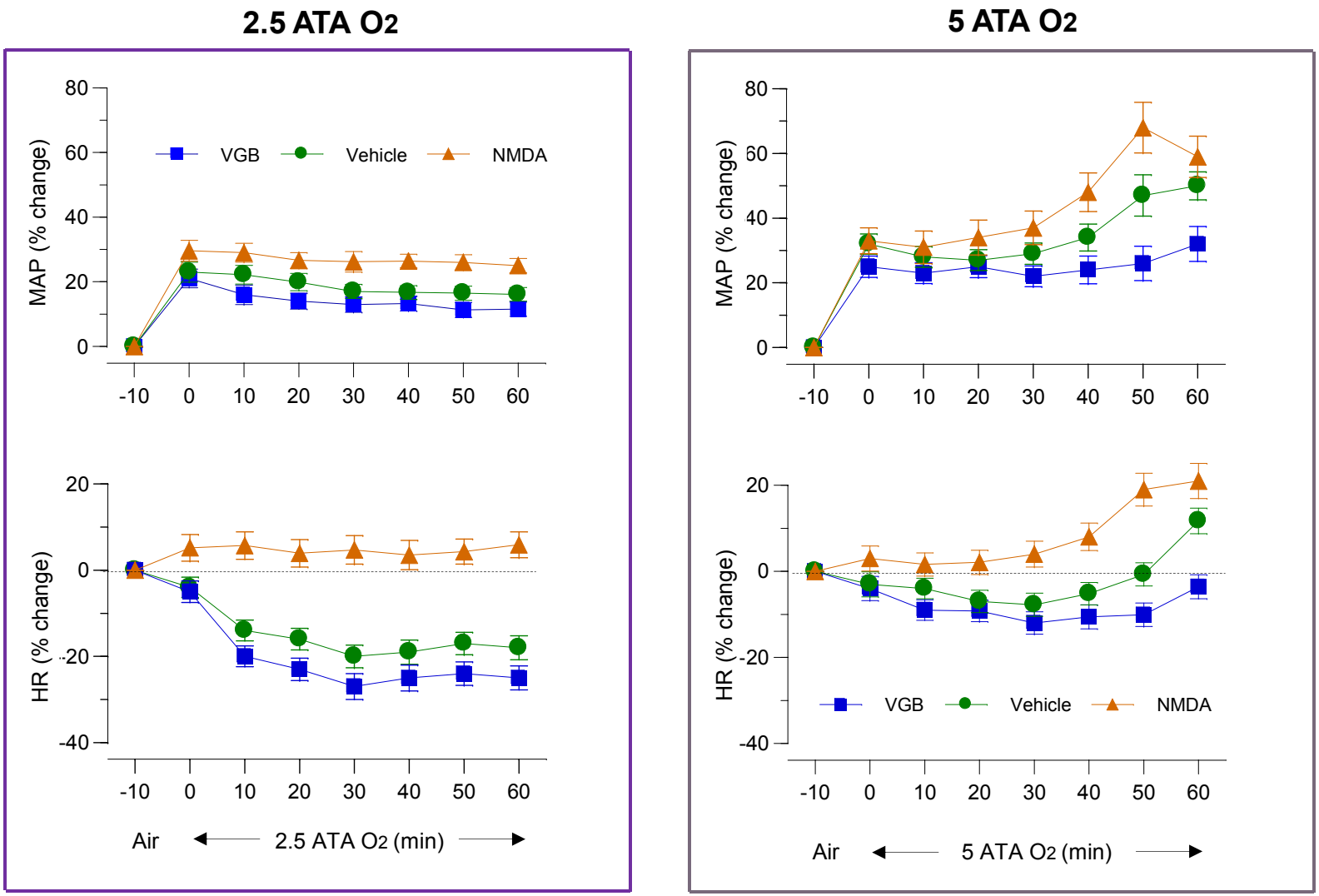
EEG spikes, convulsions latency

Study approach:

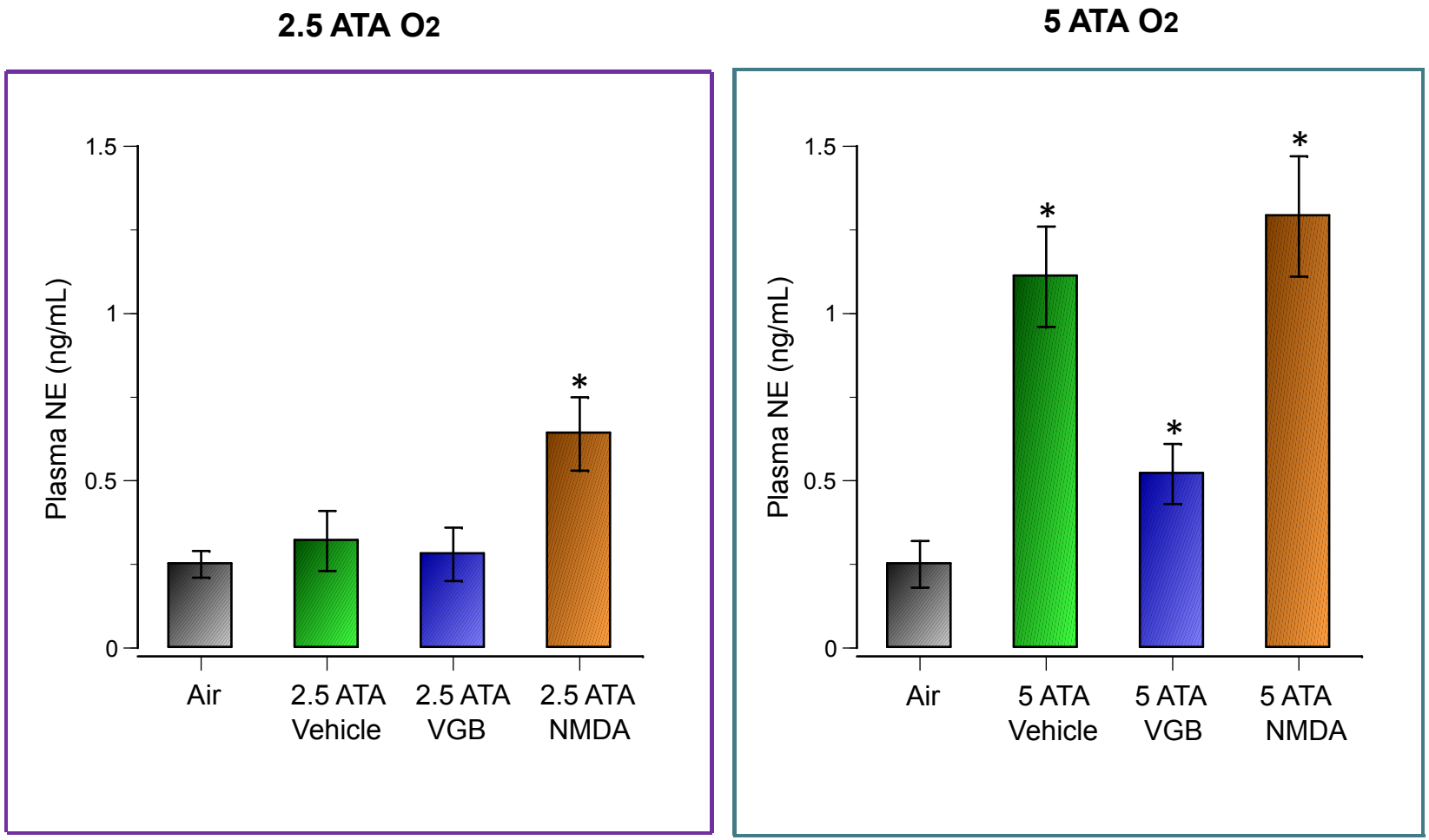
Alteration of Glutamate or GABA neurotransmission by intracerebroventricular injection of Vigabatrin or NMDA



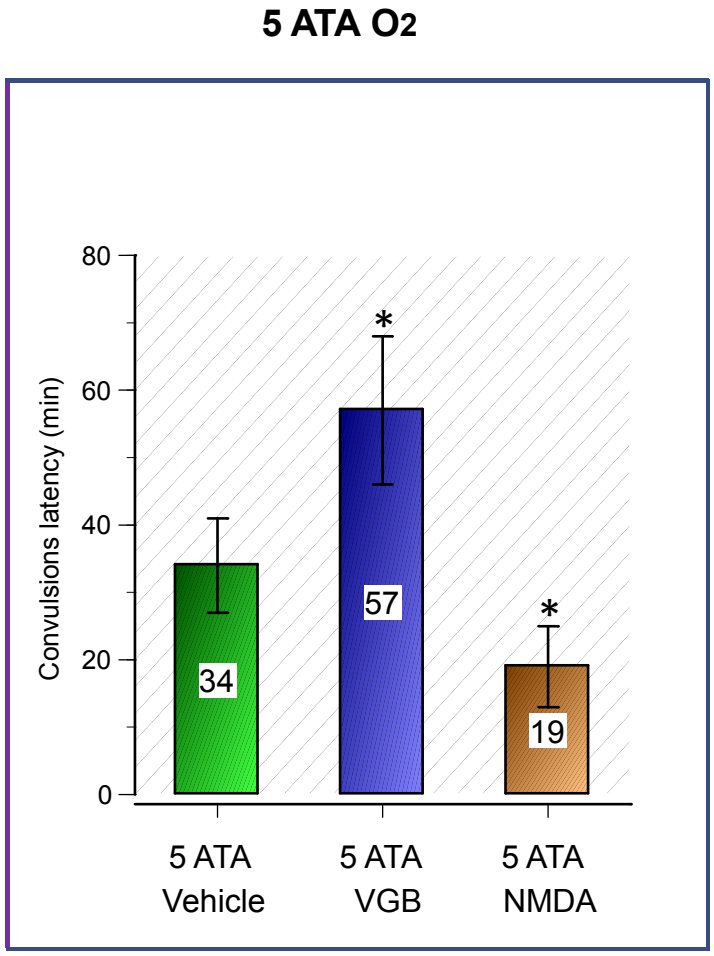
Glutamate/GABA Mediated Cardiovascular Responses to HBO_2

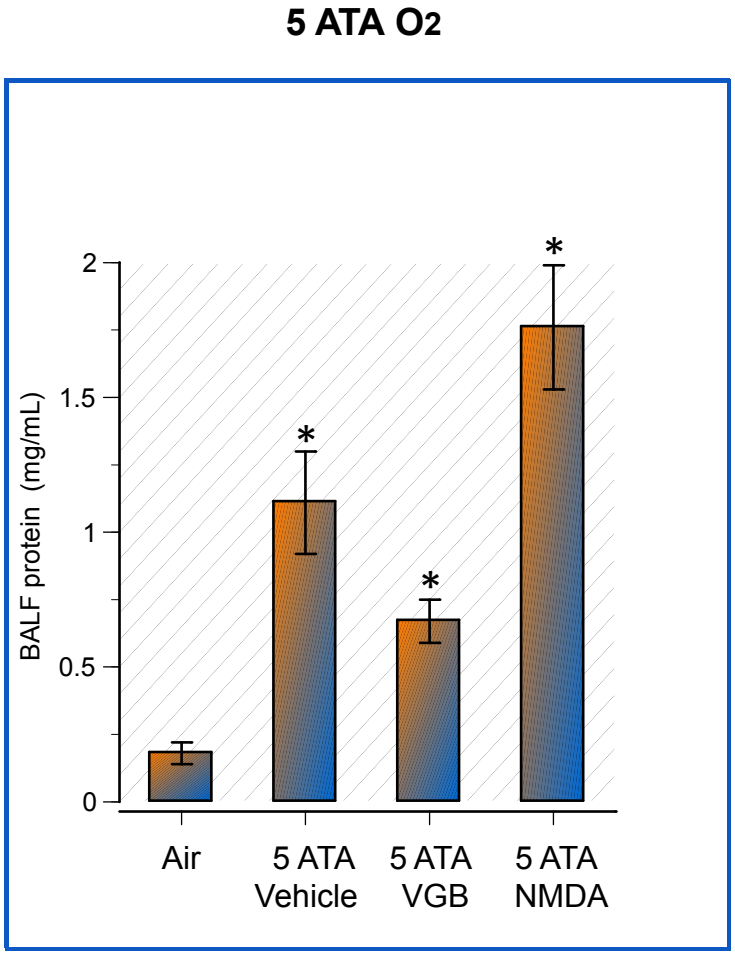


Glutamate/GABA Mediated Autonomic Responses to HBO_2

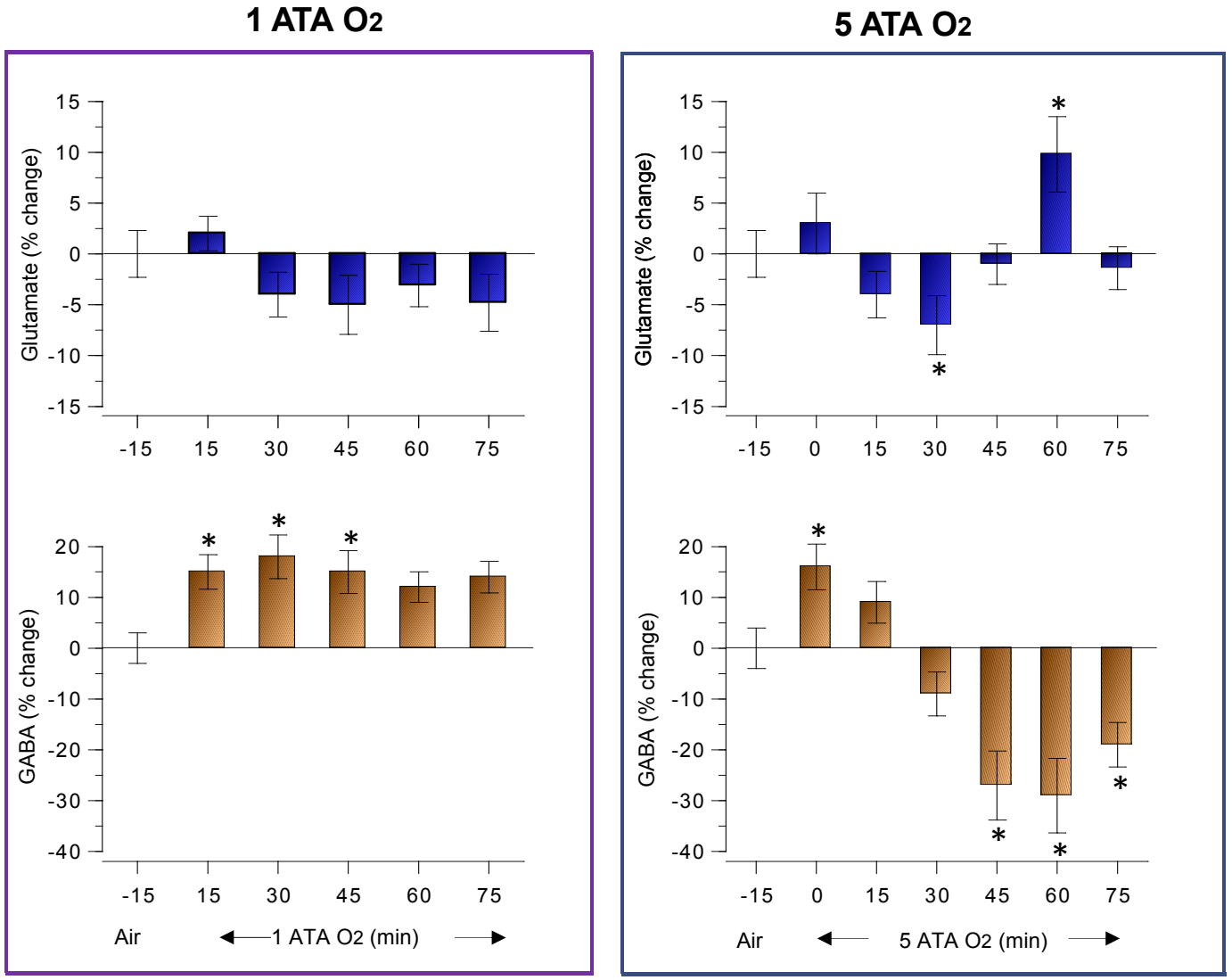


Glutamate/GABA Mediated HBO_2 Seizures and Lung Injury

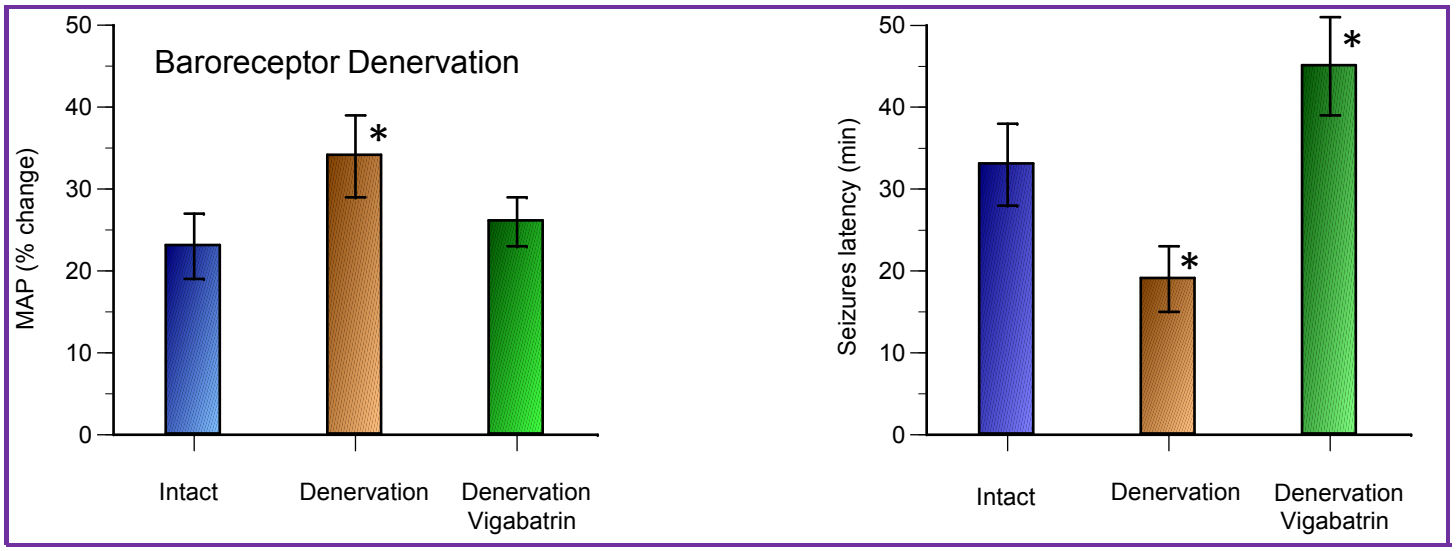


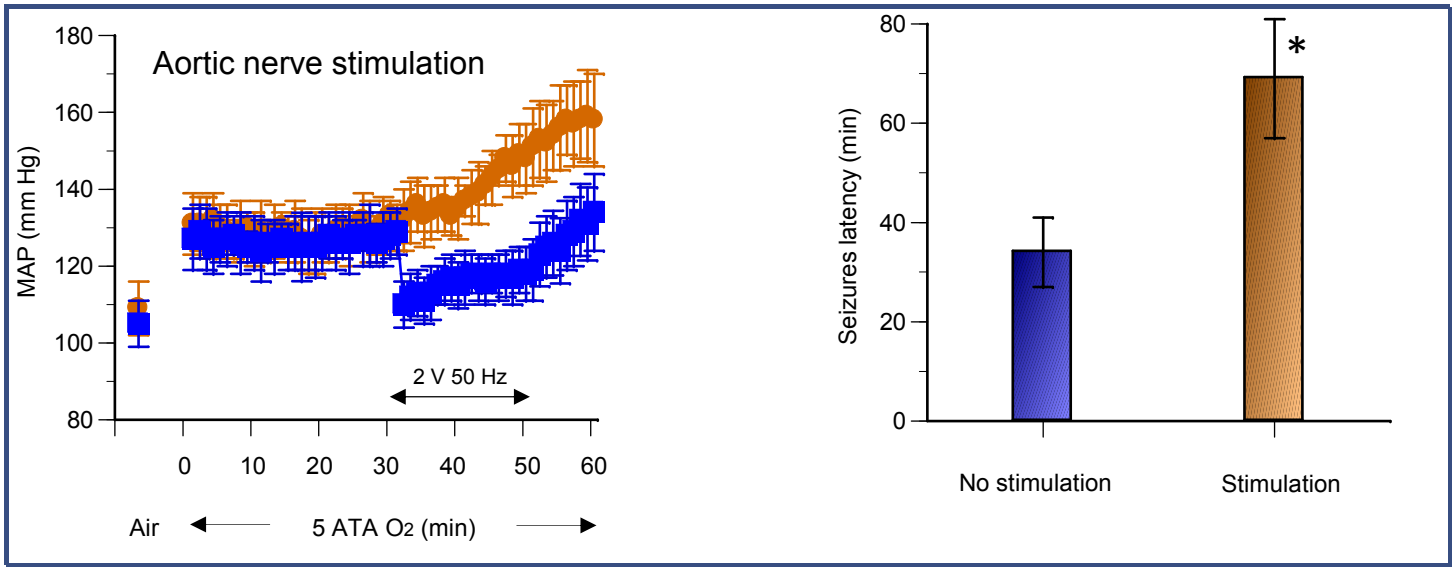


Glutamate and GABA Release in Rat Striatum in Hyperoxia

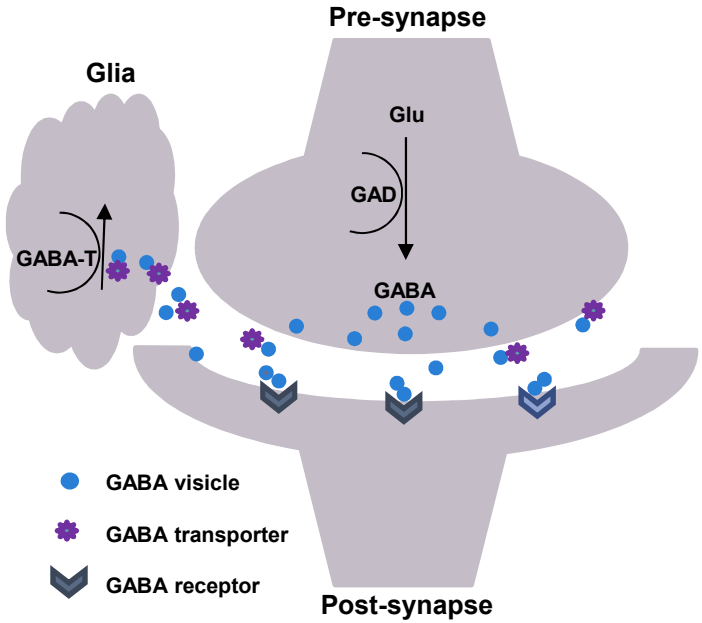


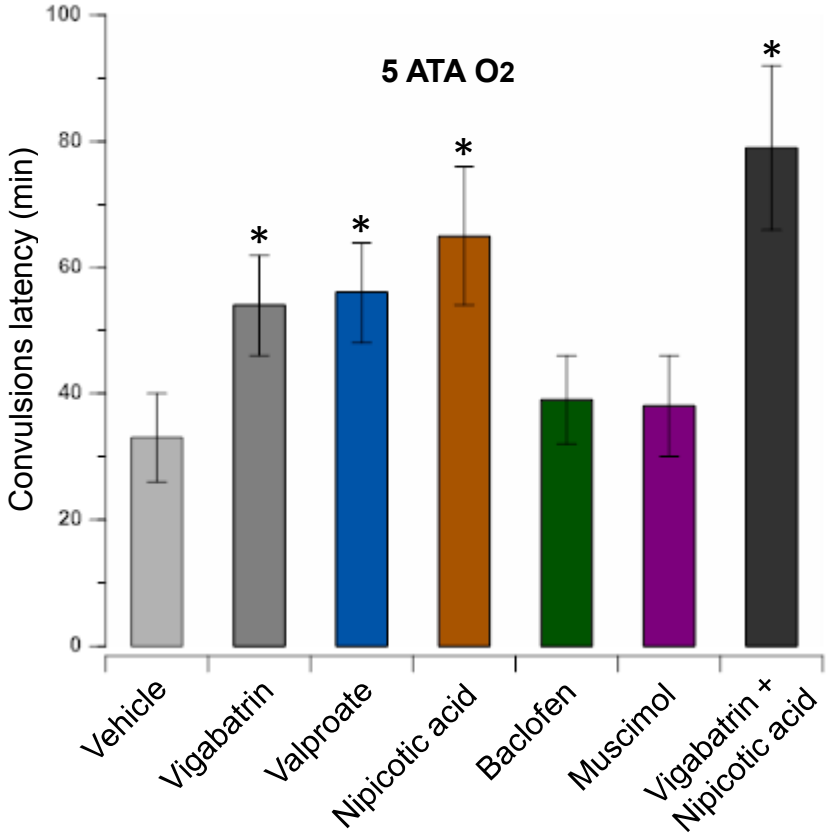
GABA Mediated HBO_2 Seizures are Modulated by Baroreceptor Activity





Effects of GABA-transmission Activation on HBO_2 related Seizures





Conclusions

- Moderate HBO_2 levels (<3 ATA) inhibit efferent sympathetic drive by baroreflex-mediated elevation of GABAergic tone.

- HBO_2 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 HBO_2 toxicity.