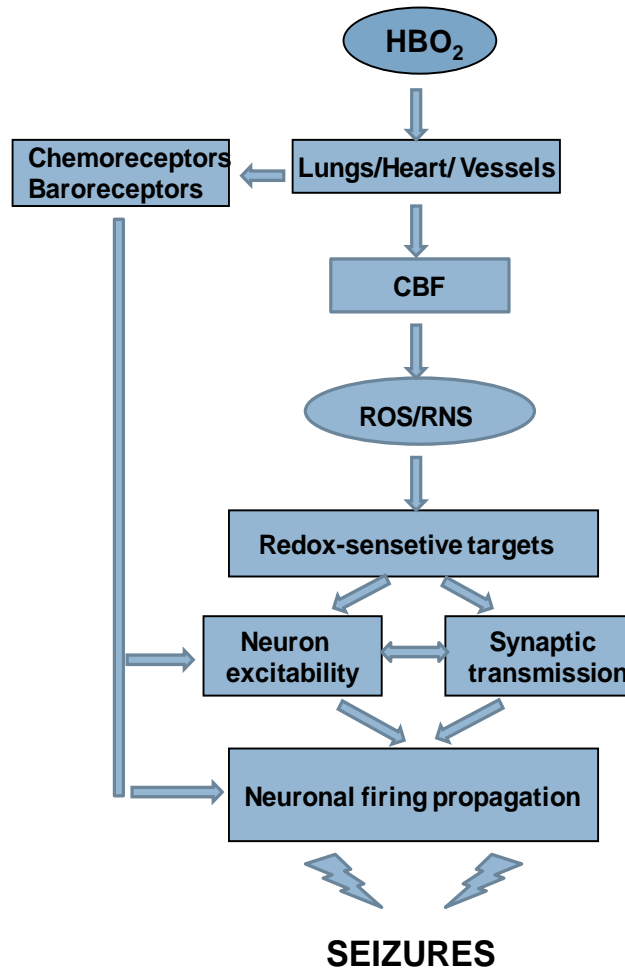


Critical Events in CNS O₂ Toxicity and Novel Approaches for Delaying Oxygen Seizures

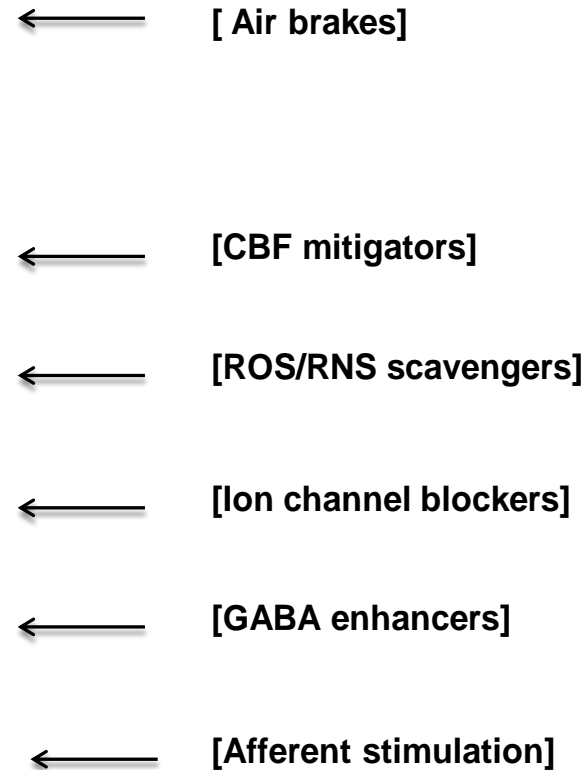
Demchenko IT, Gasier HG, Allen BW, Piantadosi CA

*Center for Hyperbaric Medicine and Environmental Physiology
Duke University Medical Center, Durham, NC 27710*

Events of Oxygen Seizures Progression



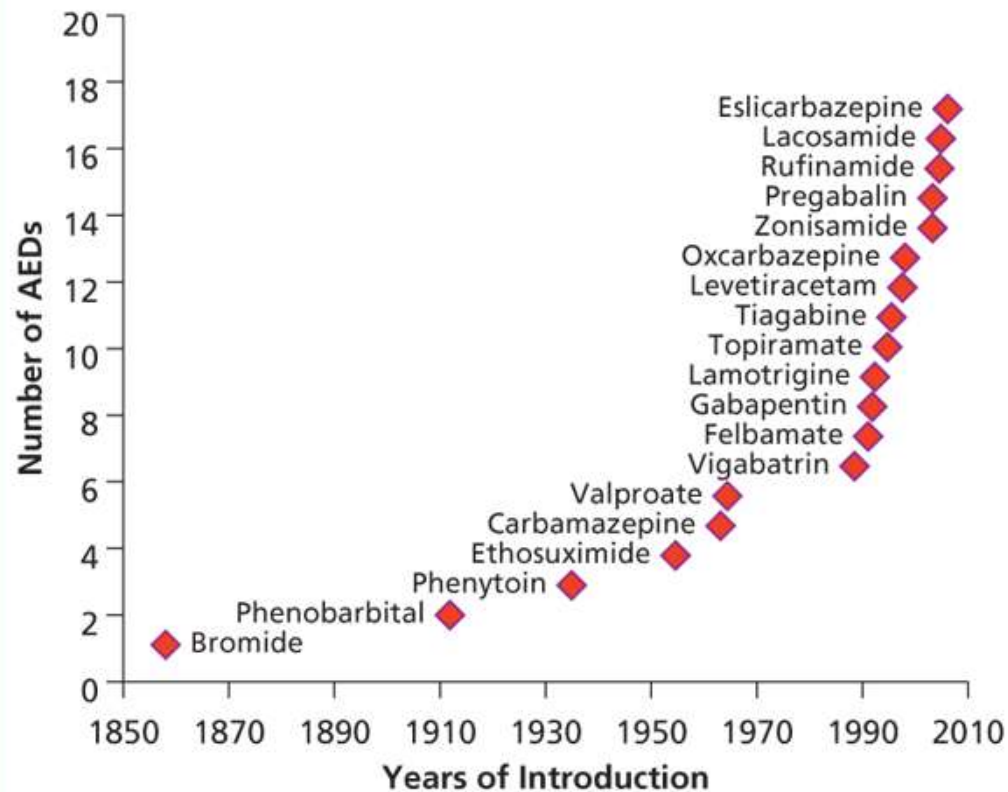
Targets for Oxygen Seizures Prevention



Aims:

- **To screen FDA-approved antiepileptic drugs (AEDs) and vasoactive agents for efficacy in preventing oxygen seizures in mice**
- **To use the selected AEDs and vasoactive agents to assess their effects on physiological responses**

Figure 1: Surge in Development of Antiepileptic Drugs Offers New Options in Epilepsy Management

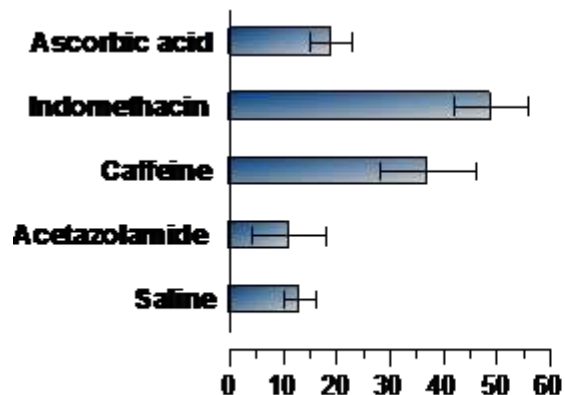


AED: antiepileptic drug.

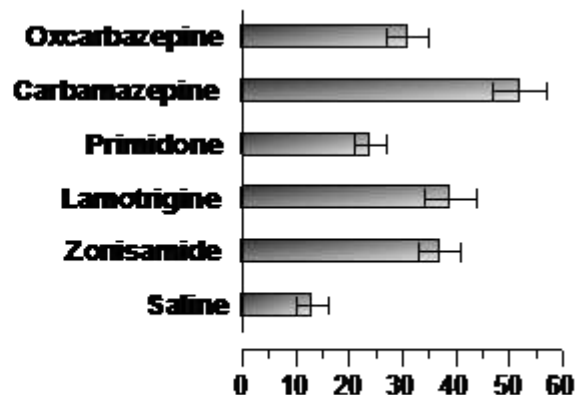
Brodie M. 9th European Congress on Epileptology (ECE 2010).
 "A new vision for epilepsy management? From key learnings
 to new developments in the next decade" Symposium.

Effects of FDA- approved antiepileptic drugs and vasoactive agents on oxygen seizures prevention in mice

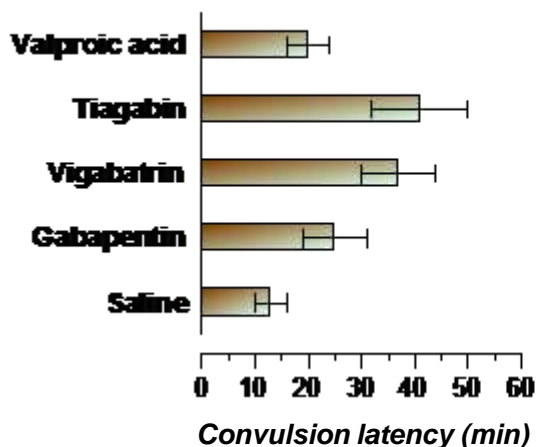
CBF mitigators:



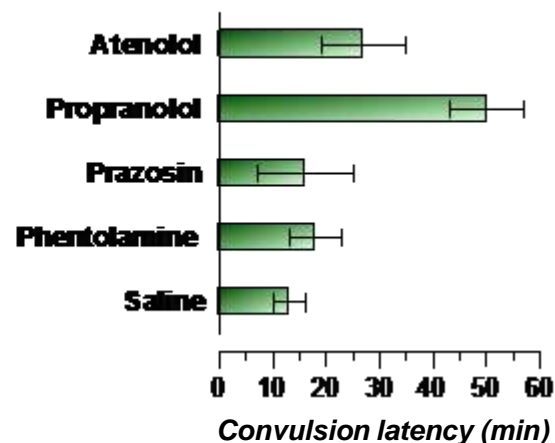
Na⁺ channel blockers:



GABA enhancers:



Sympathetic inhibitors:



Selected AEDs and vasoactive agents for assessment of physiological responses to HBO₂

Sodium Channels Blocker:

Carbamazepine [Tegretol®]
Lamotrigine [Lamictal®]

CBF Mitigators:

Indomethacin
Caffeine

GABA Enhancers:

Vigabatrin [Sabril®]
Tiagabin [Gabitril®]

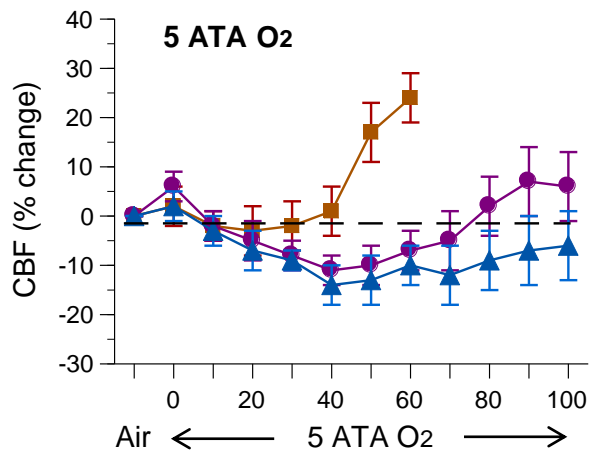
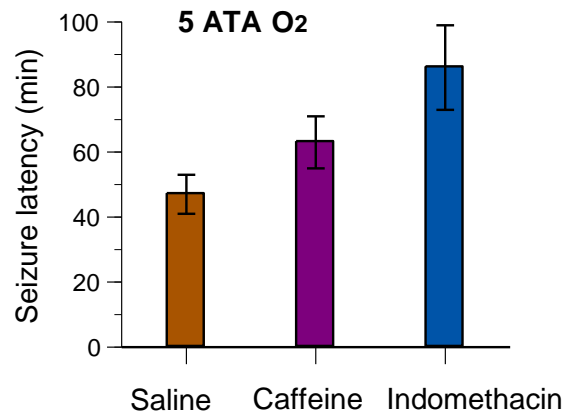
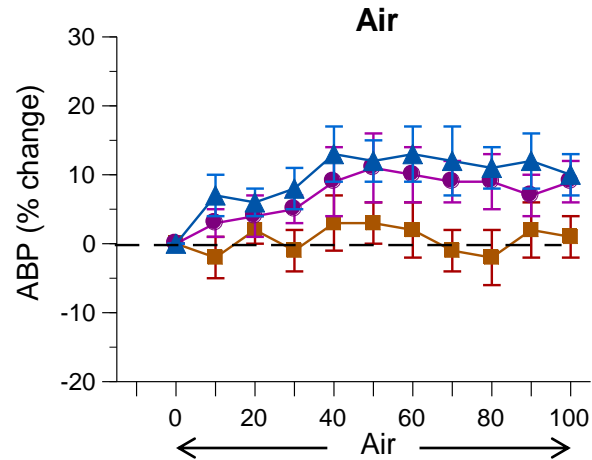
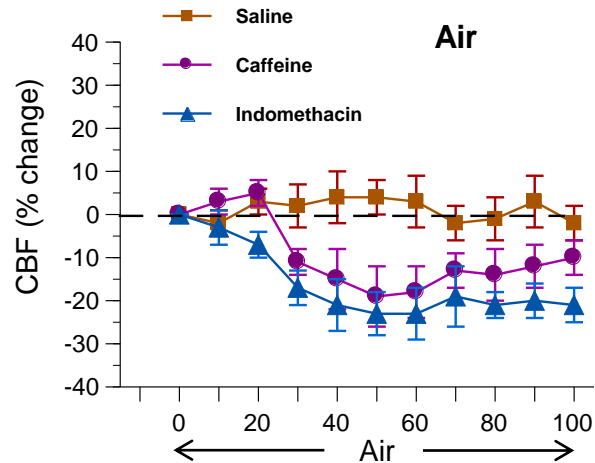
ROS scavenger:

Ascorbic acid

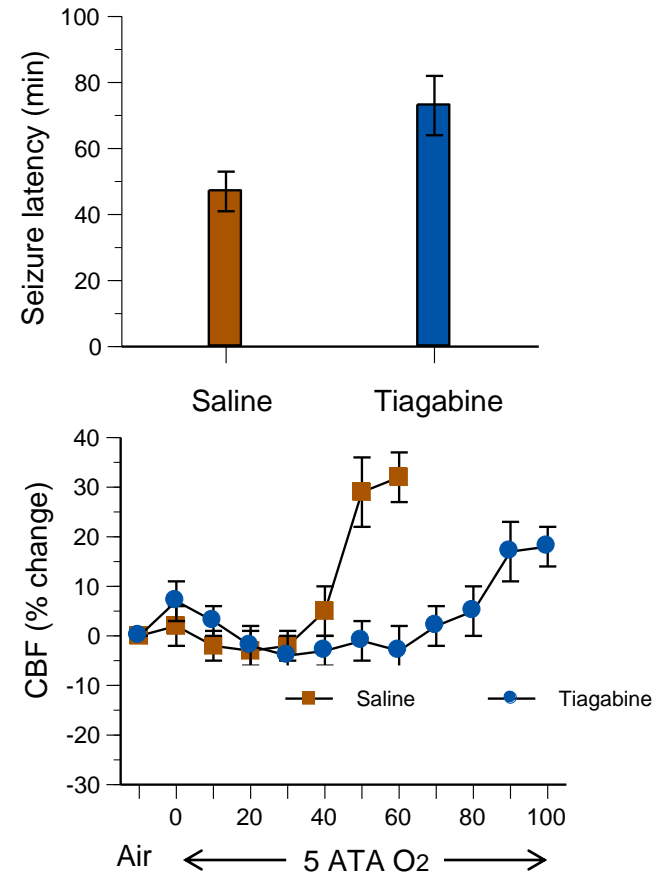
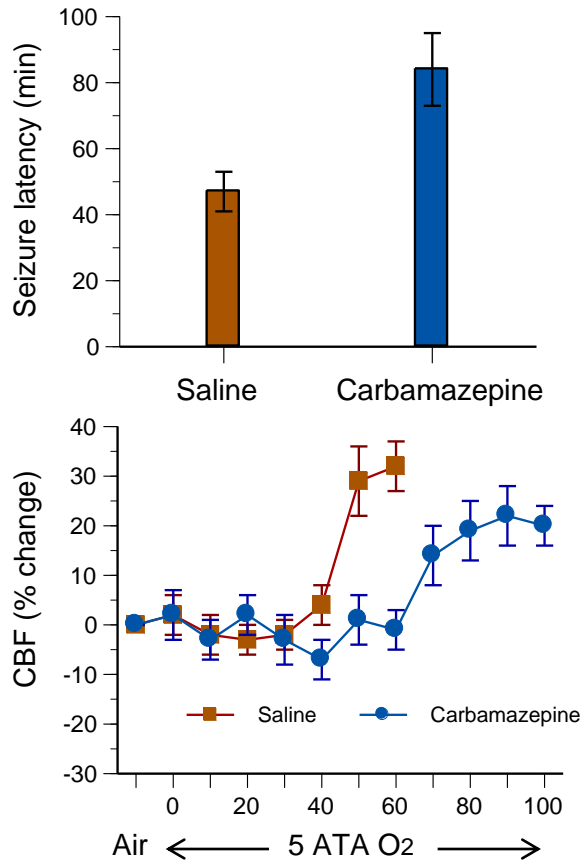
Sympathetic Inhibitor:

Propranolol

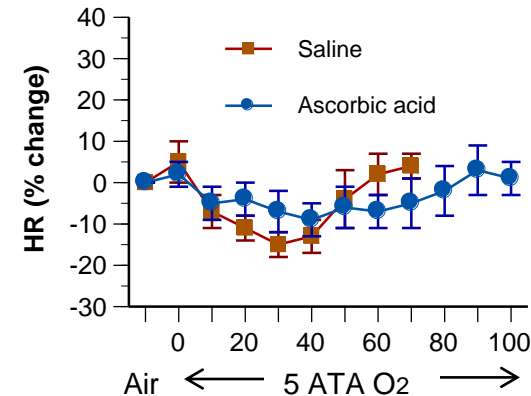
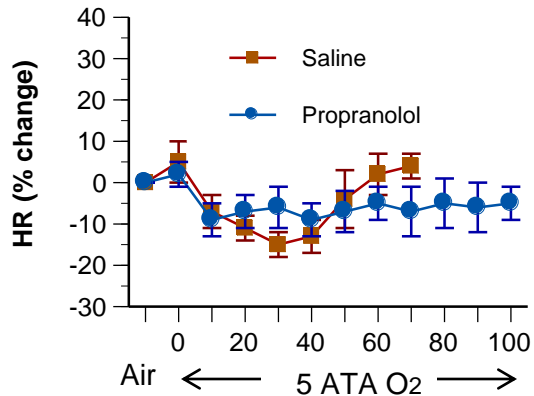
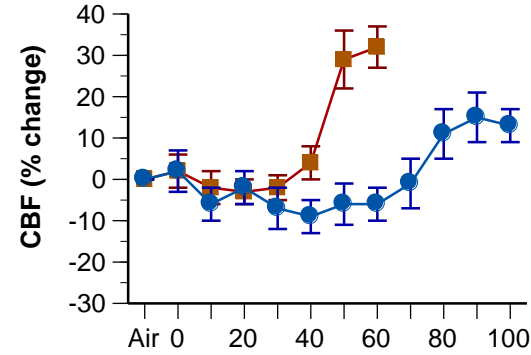
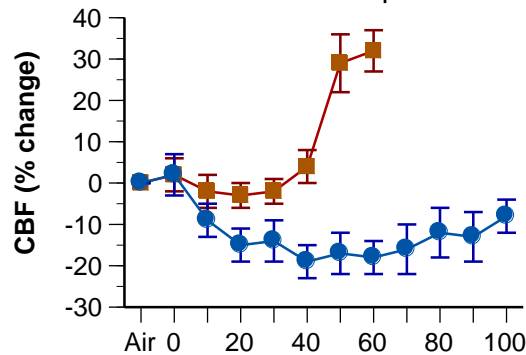
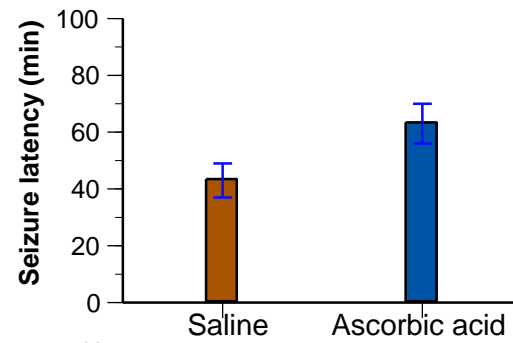
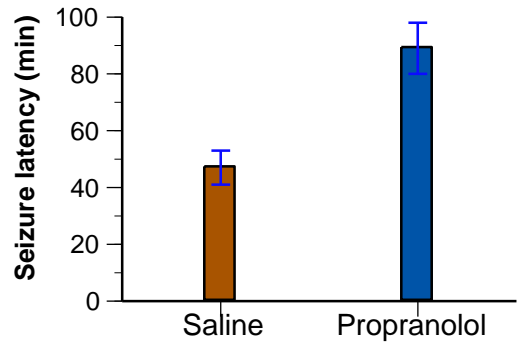
Physiological Responses to HBO₂ and Seizure Latency in Rats treated with Caffeine or Indomethacin



Physiological Responses to HBO2 and Seizure Latency in Rats treated with Carbamazepine or Tiagabine



Physiological Responses to HBO₂ and Seizure Latency in Rats treated with Propranolol or Ascorbic acid



Conclusions

- **Some FDA-approved drugs can significantly delay seizures in HBO₂**
- **Based on known mechanisms of action, these drugs can be useful for investigating mechanisms of CNS O₂ toxicity**
- **AEDs used clinically to treat epilepsy may be used for an effective pharmacologic intervention that significantly extends the safe duration for human exposed to HBO₂**