



Clonidine Does Not Prevent Pulmonary Injury in Conscious Rats Exposed to Hyperbaric Oxygen

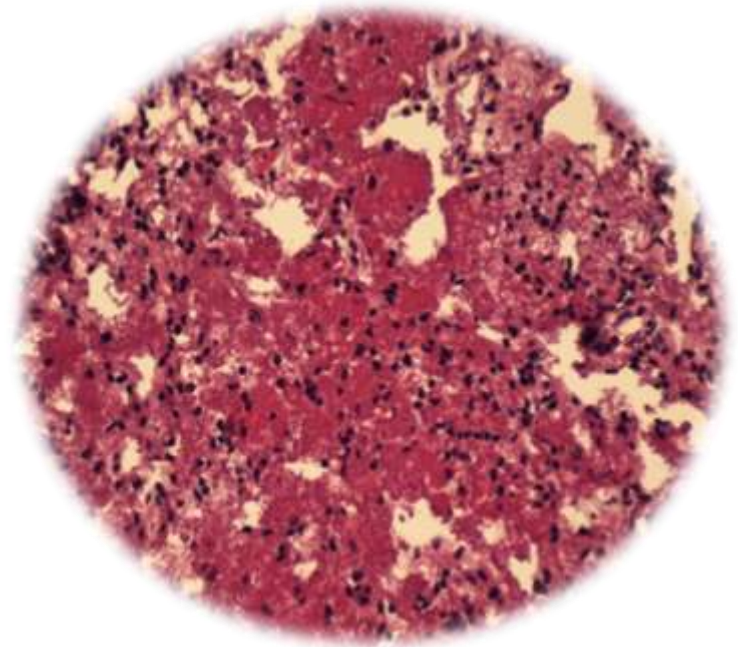
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Background

Neurogenic pulmonary injury

1. Central sympathetic excitation
 - a) Increased heart rate
 - b) Increased plasma norepinephrine
 - c) Increased sympathetic activity (RSNA)
2. Left ventricular dysfunction
 - a) Decreased stroke work
3. Pulmonary hypertension
 - a) Increased right ventricular systolic pressure and left ventricular diastolic pressure
4. Capillary damage leading to transudation of fluid, protein and red blood cells



Light micrograph (20x) of a mouse lung from an animal exposed to 4 ATA O₂ for 100 min that displayed symptoms of CNS O₂ toxicity.

Demchenko IT et al. Am J Physiol Lung Cell Mol Physiol 2007; 293:229-238.

Demchenko IT et al. Am J Physiol Lung Cell Mol Physiol 2011; 300:102-111.

Demchenko IT et al. J Appl Physiol 2012; 112:1814-1823.

Objective

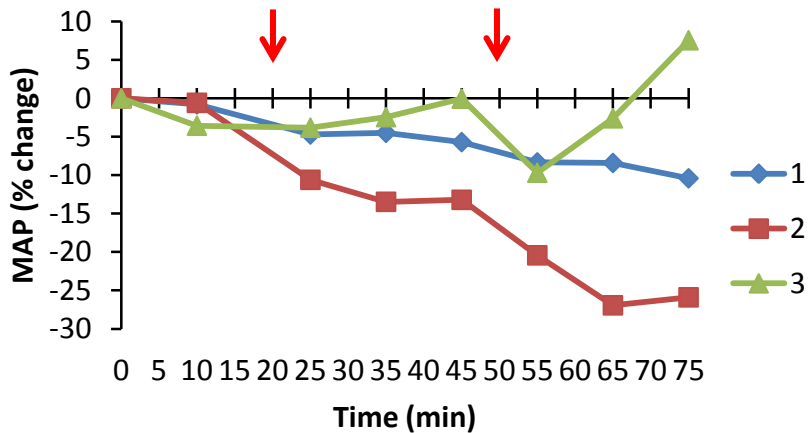
- By reducing central sympathetic output, acute lung injury may be preventable during HBO₂.
- Determine whether clonidine (α_2 -adrenoceptor agonist that inhibits central sympathetic nerve activity) increases seizure latency and prevents acute lung injury in rats exposed to HBO₂ at 5 and 6 ATA.
- **Hypothesis:** Seizure latency would be increased and acute lung injury lessened following clonidine administration.

Methods

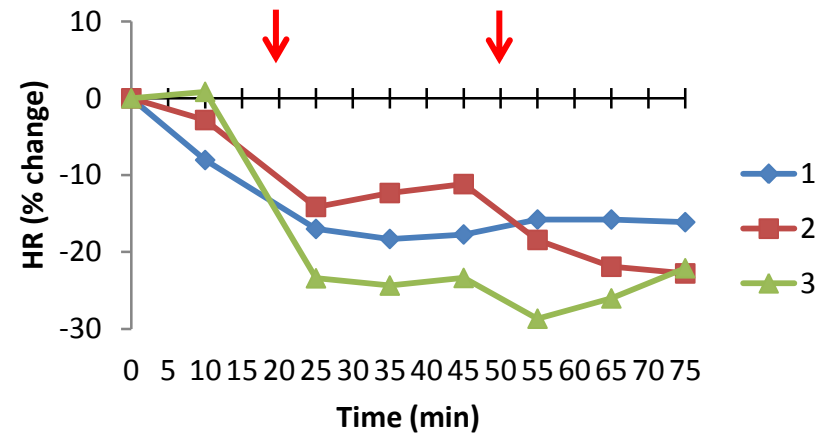
- **Animals:** Sprague-Dawley rats (270-338 g)
- **HBO₂:** 5 (*n* = 6) and 6 ATA (*n* = 6)
- **Clonidine HCl:** 10 µg/kg (*n* = 3) and 30 µg/kg (*n* = 3)
- **CNS O₂ toxicity:**
 - Seizure latency
- **Acute lung injury:**
 - Post-mortem examination:
 1. Absent = 0
 2. Mild = 1
 3. Moderate = 2
 4. Severe = 3
 - Bronchoalveolar lavage fluid (BALF):
 1. LDH
 2. Total protein
 3. Total nitrite/nitrates (NO_x)

Hemodynamics at 6 ATA

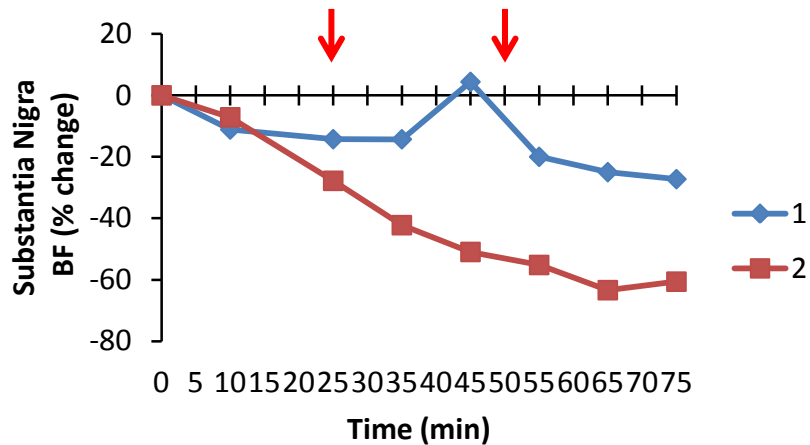
↓ = i.v. clonidine
administration (5 $\mu\text{g}/\text{kg}$)



Mean decrease: ~6% following first
and ~12% following second injection

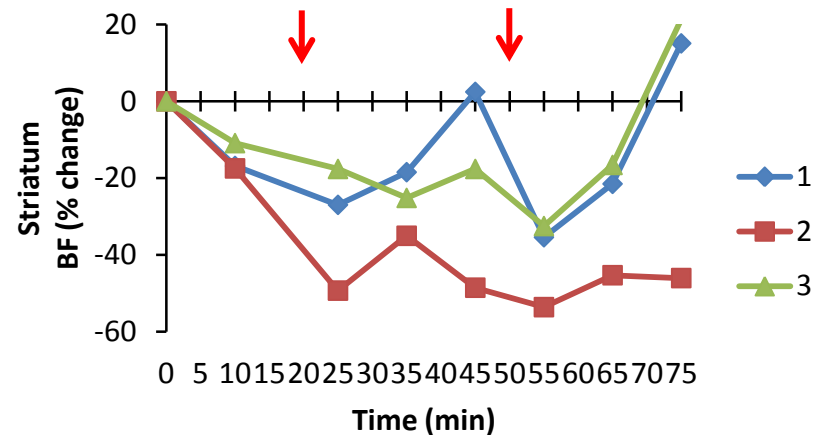


Mean decrease: ~18% following first
and ~20% following second injection

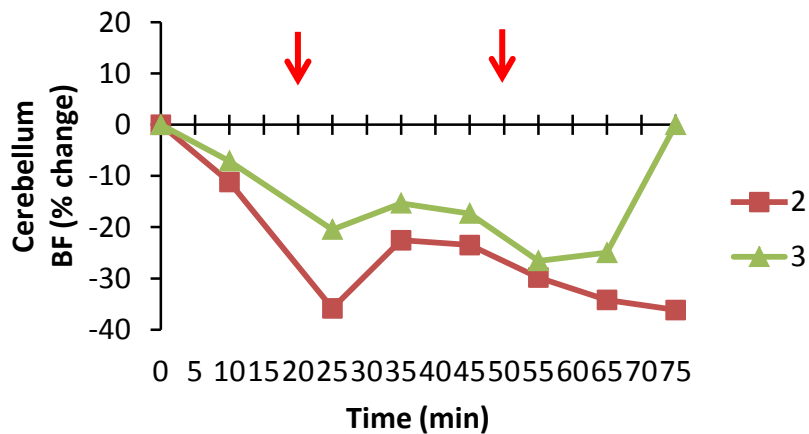


Mean maximum decrease
~44% at 65 min

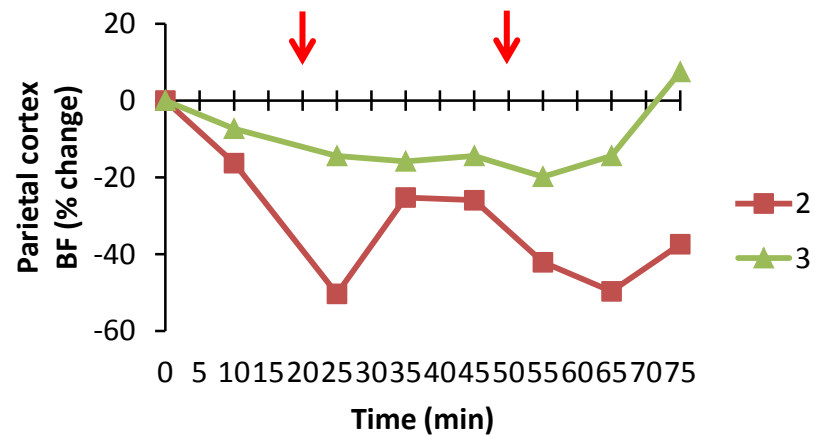
↓ = i.v. clonidine
administration (5 µg/kg)



Mean maximum decrease
~40% at 55 min



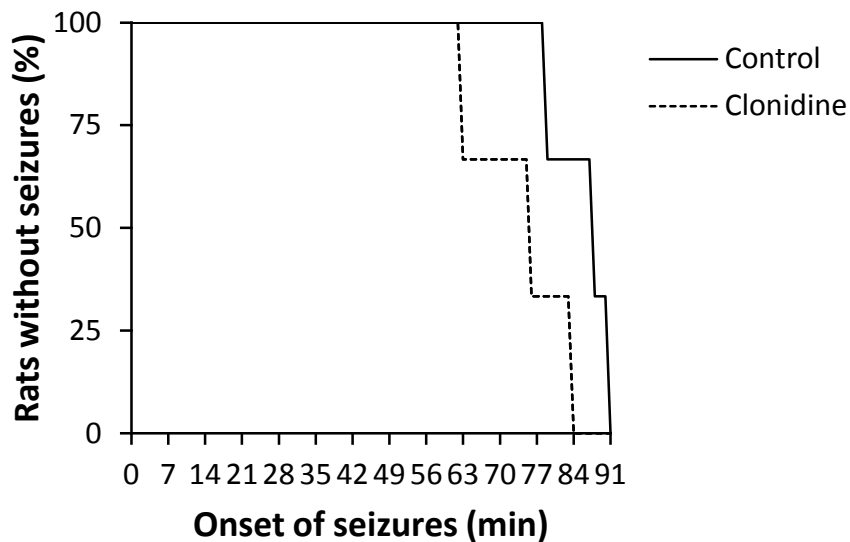
Mean maximum decrease
~30% at 65 min



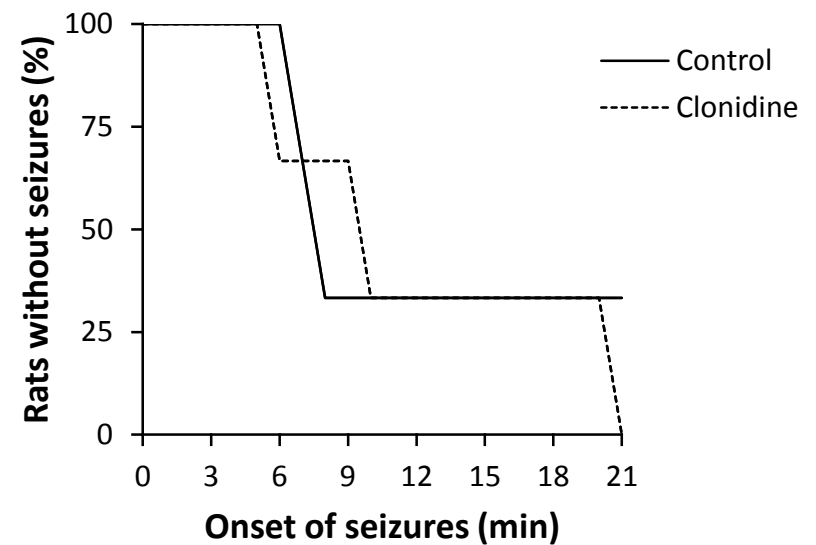
Mean maximum decrease
~32% at 65 min

Seizure latency

5 ATA for 91 min



6 ATA for 21 min



All animals displayed symptoms of CNS O₂ toxicity at both HBO₂ exposures, and 83.3% of control and 100% of the clonidine animals exhibited tonic-clonic seizures.

Acute lung injury

Group	<i>n</i>	HBO ₂	Mean acute lung injury score
Control	3	5 ATA	2
Clonidine (10 µg/kg)	3	5 ATA	3
Control	3	6 ATA	3
Clonidine (30 µg/kg)	3	6 ATA	2

$p > 0.05$; Mann-Whitney U test

BALF Biomarkers of Acute Lung Injury and Inflammation

Biomarker	Control (<i>n</i> = 6)	Clonidine (<i>n</i> = 6)
LDH (units/L)	43.6 ± 24.9	60.0 ± 31.7
Total protein (mg/mL)	1.3 ± 1.5	3.4 ± 1.9
NOx (μmol/L)	10.6 ± 5.3	13.7 ± 7.8

Values are means ± SD. $p > 0.05$ (t-test).

Summary/Conclusions

- Clonidine administration (10-30 $\mu\text{g}/\text{kg}$) does not appear to protect against symptoms of CNS O_2 toxicity or acute lung injury in rats exposed to HBO_2 at 5-6 ATA.
- These preliminary results suggest that high sympathetic outflow does not shorten seizure latency or act as the sole driver of neurogenic pulmonary damage.

Acknowledgements

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