

WG 7 (Naval and Undersea Medicine)

## Synergistic Neuroprotection by Caffeine and Astaxanthin Against CNS-OT

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### Background:

Central nervous system oxygen toxicity (CNS-OT) is a critical concern for Navy divers using closed-circuit rebreathers who are subjected to prolonged exposure to hyperbaric oxygen levels. We explored the potential of specific dietary supplements, caffeine, and astaxanthin, to delay the onset of CNS-OT.

### Methods:

Experiments were conducted using male C57BL/6 mice exposed to pure oxygen at 507 kPa, with latency to tonic-clonic seizures recorded. Mice were orally administered caffeine (1.25, 2.5, or 5 mg/kg), astaxanthin (8 mg/kg), or a vehicle (water).

### Results:

Caffeine and astaxanthin significantly extended the latency period to seizure onset ( $P < 0.03$ ). Notably, combining caffeine and astaxanthin ( $P < 0.001$  vs. control) provided better protection against CNS-OT than either substance alone.

### Conclusions:

Our results suggest that administering caffeine and astaxanthin before hyperbaric oxygen exposure delays hyperoxia-induced seizures. We aim to translate this work to a human model, with a focus on expanding oxygen dive profiles for combat divers by extending depth, duration, and range.

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## Examining the Potential of Hyperbaric Oxygen Therapy to Treat Post Traumatic Stress Disorder

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### Background:

Post-Traumatic Stress Disorder (PTSD) affects over 6% of the general population with a lifetime prevalence as high as 33% in high-risk populations - including veterans, combat zone residents and areas affected by natural disasters. Defined as the administration of breathing oxygen at partial pressures exceeding 1 atm, hyperbaric oxygen (HBO) therapy has been attempted in various neurological and psychiatric impairments. Hyperoxemia, with PaO<sub>2</sub> as high as 1800mmHg under 3.0 ATA of pure O<sub>2</sub>, is the most important mechanistic path by which HBO alters physiology. A recent pooled estimate of 4 RCTs totaling 252 patients found no significant effect of HBO therapy compared with sham (PCL Md of 0.61, 95% CI [-7.75, 8.96],  $p = 0.38$ ). (1)

### Goals:

Our primary goal is to examine the effect of HBO therapy on PTSD symptoms.

### Materials and Methods:

In this double blinded, prospectively randomized, sham controlled, pragmatic cross over study patients referred by our VA are randomized to either one of two treatment protocols (2.0 ATA and 2.5 ATA) or placebo (a sham protocol) for 60 daily sessions. To be included, patients must be 18-80 years old with a PTSD (as per DSM-5 criteria) severe enough to warrant a military discharge. Excluded are patients with known or suspected psychosis or suicidality and any contraindication to HBO. The Clinician-Administered PTSD Scale (CAPS)-5 score at the end of the treatment series compared to the baseline score is the primary outcome with various questionnaires and biometric sleep recording serving as secondary and exploratory outcomes, respectively.

### Discussion points:

We hypothesize that symptoms of PTSD will reach peak improvement following 40-60 HBO treatments compared to sham pressurized controls, with better overall improvement in higher doses of PO<sub>2</sub>, in patients with shorter duration of symptoms and when TBI is present. An interim analysis is scheduled for September 2025.