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Hyperbaric Oxygen Preconditioning Induces Protection Against CNS Oxygen Toxicity By Altering ROS Scavenger Activity

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Background

As we have shown previously, repeated and frequent dives using oxygen-enriched gas mixtures might increase the risk of central nervous system oxygen toxicity (CNS-OT). This is due to the increased production of reactive oxygen species (ROS) in hyperoxic conditions, which leads to disruption of the physiological balance between ROS production and scavenging. Paradoxically, there is evidence that preconditioning to high O_2 under normobaric conditions will provide protection against hyperoxic lung injury. However, studies of the possible beneficial effect of hyperoxic preconditioning on CNS-OT are few and far between. ***Purpose***: To examine the hypothesis that preconditioning to hyperbaric O_2 (HBO) will provide protection against CNS-OT in the rat.

Methods

One week after baseline measurement of ROS scavenger activity, the 15 rats in the experimental group were exposed to 1h of HBO at 202 kPa for preconditioning once every other day for a total of three sessions. The rats in the control group (n=15) were kept in air under normobaric conditions. Twenty-four hours after preconditioning, the rats in both groups were exposed to 608 kPa. Immediately thereafter the animals were sacrificed, and samples were taken from the blood, brain, and heart.

Results

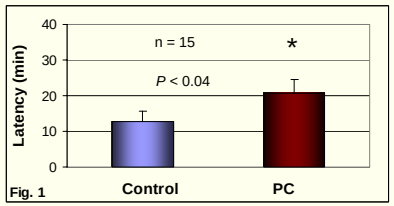
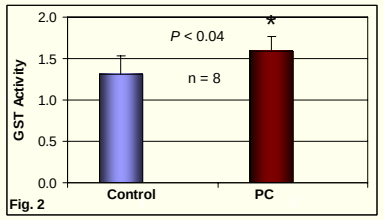
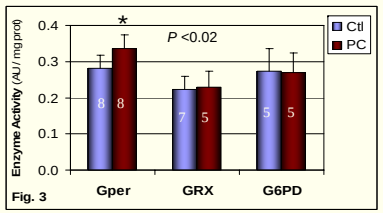
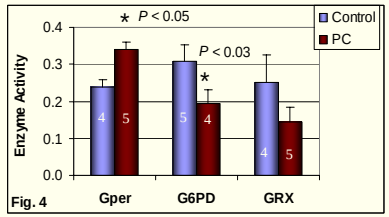


Fig. 1: Latency to CNS-OT was almost twice as long in preconditioned (PC) rats. Results are presented as mean ± S.D. in all figures.

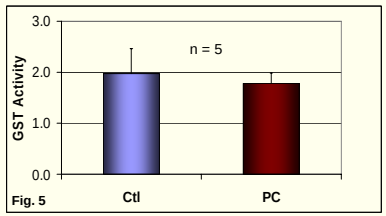


Figs. 2, 3: There was a significant increase of approximately 20% in the activity of glutathione-S-transferase (GST, Fig. 2) and glutathione-peroxidase (Gper, Fig. 3) in the cortex of PC rats.





Figs. 4, 5: There was a significant decrease in the activity of GRx and G6PD in the hippocampus (30 and 37%, respectively) after HBO preconditioning, whereas there was a significant increase of 42% in the activity of Gper (Fig. 4). There was an insignificant decrease of 9% in GST activity in the hippocampus after preconditioning (Fig. 5).



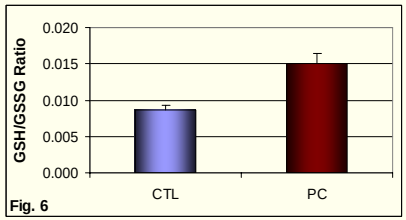


Fig. 6: There was an increase in the level of GSH in PC rats, and hence an increase in the GSH to GSSG ratio.

Conclusions

- This study demonstrates that under well defined conditions, repeated exposure to pure oxygen at 202 kPa may have a preconditioning effect, providing protection against CNS-OT.
- The mechanism by which this protection is induced involves changes in the activity of mitochondrial ROS scavenger enzymes in both the hippocampus and the cortex.
- The increase in the activity of Gper and GST may accelerate the neutralization of H_2O_2.
- The increase in the activity of Gper is borne out by the increase in the GSH to GSSG ratio in the hippocampus of PC rats.
- The reduction in the activity of G6PD in the hippocampus may result in decreased superoxide production via a drop in the production of NADPH.

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