Hyperbaric oxygen therapy as a tool for reducing the mitochondrial pathway of apoptosis in a rat model of traumatic brain injury

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Introduction

Traumatic Brain Injury (TBI) is the leading cause of death and disability in young adults. TBI can be divided into primary injury, the immediate and nonreversible mechanical damage that occurs at the moment of impact, and secondary injury, characterized by delayed death of damaged yet viable brain tissue. Within the spectrum of therapeutic modalities that have been evaluated for preventing and reducing secondary post-traumatic neuronal death, hyperbaric oxygen therapy (HBOT) has recently emerged as a potentially valuable though neglected therapeutic tool. However, since HBO (Hyperbaric Oxygen) therapy has not been implemented into the therapeutic armamentarium, little data exist regarding this Treatment's mechanism and its effects on several aspects.

Study purpose

Evaluation of hyperbaric oxygen on traumatic brain injury in several aspects:

A. Clinical and cognitive functions

B. Pathologic evaluation

Materials and methods

TBI rat model was used on 28 rats. The rats were divided into two groups: control group-TBI rats and treated group-TBI rats treated with HBO. The treated rats received HBOT 8h after injury and thereafter once every day for 5 consecutive days at a pressure of 2.5 ATA for 90 minutes. Afterward, the animals were sacrificed, and the brains were carefully removed. 7 rats were used for histological measures. All animals participated in the Cognitive-Locomotor measurements before the treatment and after it.

Results

Locomotor measurements:

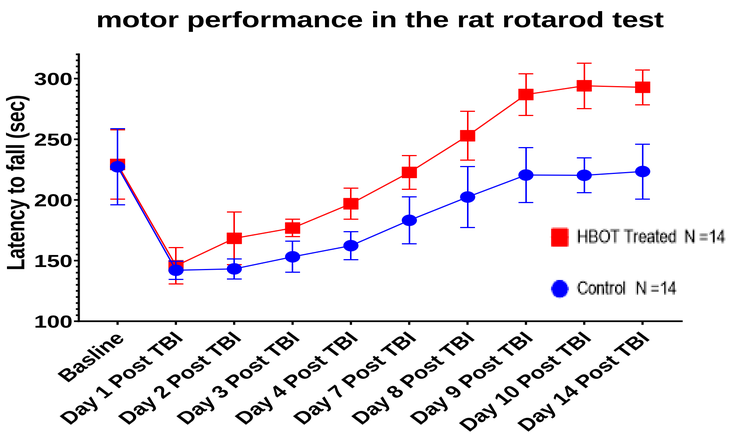

Figure 1: From day 2 post-TBI, a significant difference in the motor performance was found between the groups. HBO treated rats showed a steeper learning curve. By day 14 post-TBI, significant improvement in the performance was proven for HBO treated rats compared to this group's baseline with a significant difference.

Cognitive measurements:

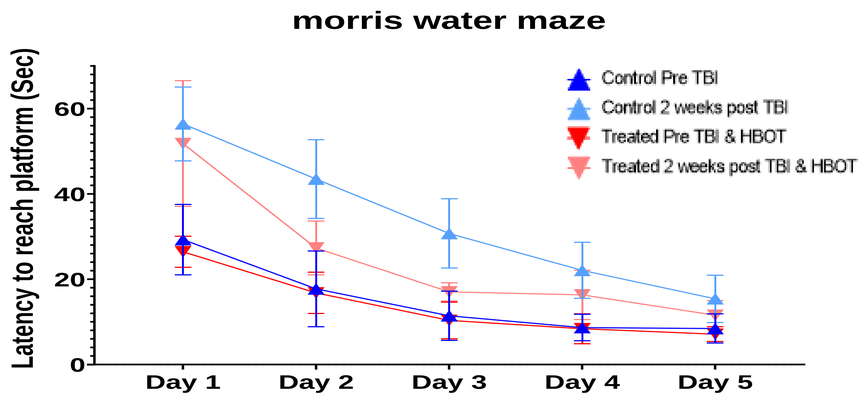

Figure 2: Control group and treated group showed no significant learning curve difference pre-TBI. Post-TBI treated group shows a steeper learning curve than the non-treated control group and significantly better results after day 2.

Histological measurements:

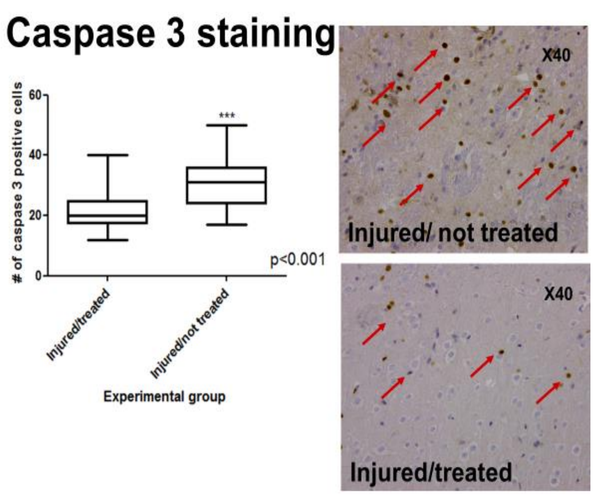

*Figure 3: Caspase 3 activity in response to Hyperbaric Oxygen treatment following traumatic brain injury (TBI). An intense increase in caspase 3 activity was observed in the injured hemisphere, which is significantly reduced in amplitude in animals that received treatment. (Means±SEM in the different groups. Asterisks indicate a significant difference at the Mann-Whitney test: *** P < 0.001 vs. non treated).*

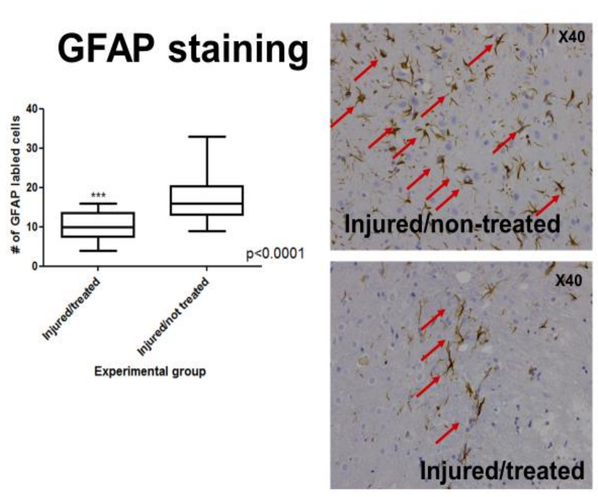

*Figure 4: GFAP staining in response to hyperbaric oxygen treatment following traumatic brain injury (TBI). A significant reduction in GFAP staining is observed in the injured hemisphere of the treated group compared to the injured hemisphere of the non treated group. (Means±SEM in the different groups. Asterisks indicate a significant difference at the Mann-Whitney test: *** P < 0.0001 vs. non treated).*

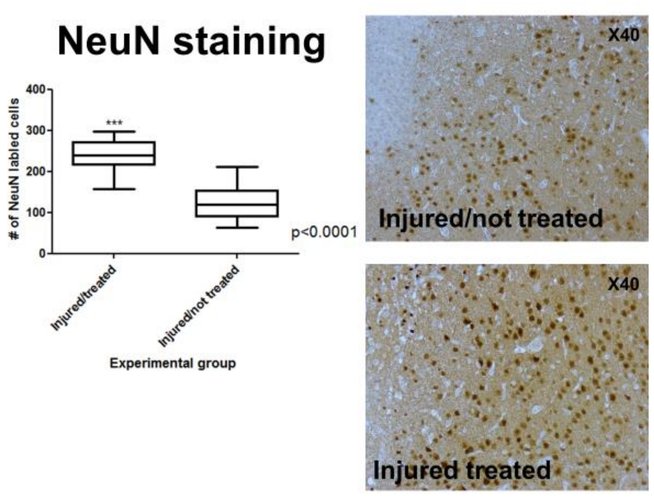

*Figure 5: NeuN staining in response to Hyperbaric Oxygen treatment following traumatic brain injury (TBI). There was a marked increase in the number of neurons in the injured hemisphere of the treated group compared to the injured hemisphere of the non treated group. (Means±SEM in the different groups. Asterisks indicate a significant difference at the Mann-Whitney test: *** P < 0.0001 vs. non treated).*

Conclusions

HBO treatment has a multi-level neuroprotective effect from the higher function such as cognitive & motor improvement through the cellular level of neurons survival to the restoring of mitochondrial function.