Multiparametric MRI characterization of NBO treatment following mild Traumatic Brain Injury

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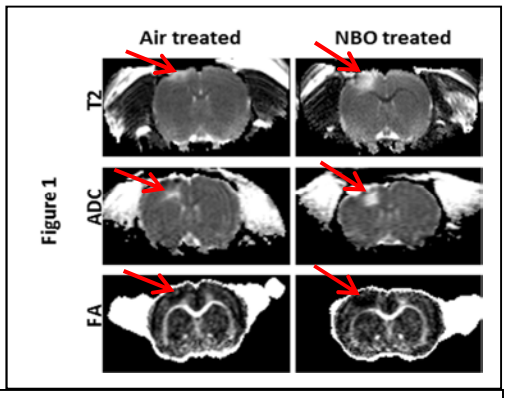
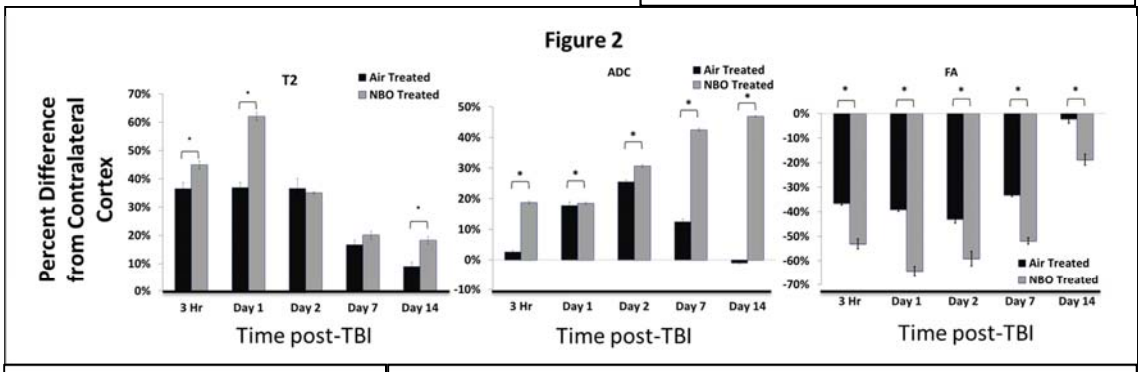
Target audience: Researchers studying Traumatic Brain Injury

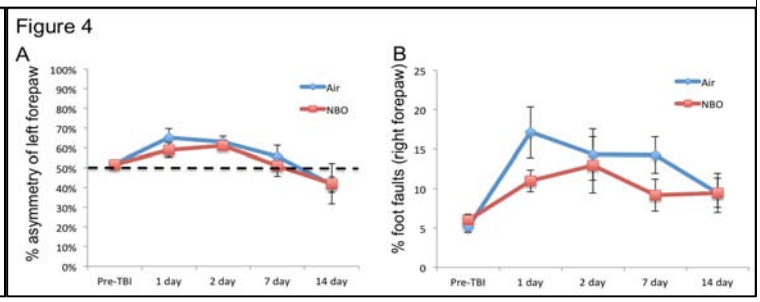
Purpose: The goal of this study was to investigate the novel neuroprotective effect of normobaric oxygen (NBO) on mild traumatic brain injury (TBI) using multimodal MRI.

Methods: Anesthetized male rats (275-350g) were placed in a stereotaxic frame and a 6mm craniotomy over the left primary motor/somatosensory cortex region exposed the intact dura matter. The dura was impacted directly using a pneumatic cortical impactor with an impact velocity of 5.0m/s, a 250**µ**s dwell time, and 1mm depth to mimic a moderate TBI. A double-blinded randomized design was utilized. Air (n=5) or NBO (100% FiO_2) (n=5) was administered 0.5 to 3.5 hrs post TBI induction. Longitudinal MRI (T2, ADC, FA) was performed on the day of the TBI, and again on days 1, 2, 7 and 14 after TBI onset.



Results & Discussion: **Figure 1** shows representative T2, ADC and FA maps of an air- and NBO treated TBI animal 2 days following injury. The lesioned area for each representative map are demonstrated by the red arrows. **Figure 2** shows the time evolution of T2, ADC, and FA of the S1 region in air- and NBO-treated animals. In air-treated TBI rats the ipsilesional T2 was elevated from contralesional T2 at 3 hrs, and day 1 and 2 but returned toward contralesional values on days 7 and 14. NBO-treatment exaggerated ispilesional T2 within 3 hours and this further increased on day1, and returned to those of air-treated animals by day 2 but remained significantly increased compared to air-treated animals on day 14. Compared to contralesional ADC, the ipsilesional ADC in air-treated animals increased acutely, peaked on day 2 and then returned toward contralesional values by day 14. In contrast, ipsilesional ADC was extremely elevated in NBO-treated animals at 3 hrs, and continued to steadily increase through day 14, with significant increases compared to air-treated animals at all time points. The increased ADC values suggest more prevalent and persistent edema formation following NBO treatment. Compared to contralesional FA, the ipsilesional FA was significantly lower at 3 hrs, and continued to decrease through day 14 in both air and NBO-treated animals. NBO-treated animals were significantly decreased compared to air treated animals at all time points. **Figure 3** shows representative air- and NBO-treated brains that were extracted 14 days post TBI. In contrast to air-treated animals, the NBO-treated animals had marked brain tissue loss in the area of the initial impact (S1 cortex). Asymmetry and foot fault tests show deficits in functional outcome measures following TBI (**Figure 4**). The % asymmetry showed both the vehicle and NBO treated rats became left forepaw dominant. The % foot faults also demonstrated an increase in the number of right foot faults in both treatment groups. There were no significant difference between NBO and vehicle treated rats at all time points explored.





Conclusion: TBI-induced edema peaked at day 2 and resolved substantially by day 7 and 14 in air-treated animals. The reduction in edema by day 14 in air-treated animals is in general agreement with improvement in the behavioral scores. NBO treatment exacerbated lesion severity as determined by T2, ADC and FA. The continual increase in ADC values in NBO-treated animals suggests more prevalent and persistent edema formation and correlates to greater lesion volume. Increased lesion volume was confirmed in NBO-treated animals when the brains were extracted and compared. However, despite the presence of increased lesion volume at day 7 and 14 in NBO-treated animals, forepaw asymmetry scores returned to normal for both groups. The data suggests that NBO-treatment increases edema formation and results in increased neurodegeneration in the impact area leading to amplified functional deficits.

REFERENCE: 1) Nair G, et. al. (2005) NeuroImage 28:165-174.