Determination of sources for evoked BOLD response under Hyperbaric Oxygen

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TARGET AUDIENCE. Neurophysiologists of hyperbaric pressure. Scientists interested in the role of O_2 on BOLD fMRI responses.

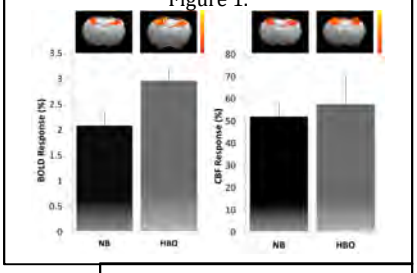
PURPOSE. Hyperbaric oxygen (HBO) therapy is used to treat a number of ailments. The goal of this study was to test two hypotheses: i) activation-induced CBF fMRI response is not dependent on hemoglobin oxygenation, and ii) activation-induced BOLD fMRI is markedly attenuated under HBO. Additional experiments were performed to evaluate the potential contributions of stimulus-evoked inflow, spin density, and electrical activity to BOLD fMRI responses under HBO. Baseline T_2^*-weighted MRI signals were analyzed in the primary somatosensory cortex (S1) and superior sagittal sinus (SSS) for multiple HBO conditions. CBF and BOLD fMRI of forepaw stimulation in anesthetized rats was performed under 3 atmosphere absolution (ATA) HBO and compared with normobaric air (NB).

METHODS. A hyperbaric chamber was constructed for use in the MRI scanner[1]. Male SD rats (n=22, 325±50g) were anesthetized with α-chloralose under spontaneous breathing conditions. Respiration and heart rate were monitored and rectal temperature maintained at 37°C. Both forepaws were stimulated simultaneously in series (0.3mA, 3Hz, 0.3ms).[2] MRI measurements were made during NB and 3 ATA HBO.

Five experiments were performed: (I) BOLD fMRI was acquired at 7T using a 2cm brain surface coil with FOV=25.6x25.6x30mm, matrix=96x96, TE=20ms, TR=3s, and 7 1.5mm thick slices. (II) fMRI with TR=10s was used to evaluate inflow effects. (III) Variable TE=20, 30, and 40ms. fMRI were done to evaluate spin density effect. (IV) T_2*-weighted MRI signals were obtained at NB, normobaric oxygen, and at 2 and 3 ATA HBO. (V) Basal and evoked electrophysiolgoical recording was made. Regions of interest (ROIs) in the S1 region were used to find percent changes between stimulation and resting periods. Statistical analysis was completed using paired t-tests with Bonferroni-Holm correction.

RESULTS and DISCUSSION. Respiration rate, heart rate, and SpO_2 under NB and HBO from 11 of 22 rats. Respiration rate (decrease) and SpO_2 (increase) were statistically different between NB and HBO as expected. Heart rate trended lower but did not reach statistical significance.

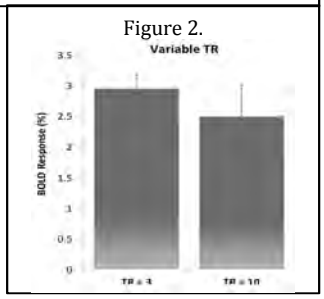
Figure 1.



Forepaw stimulation evoked reproducible CBF and BOLD fMRI responses in the bilateral primary somatosensory cortices under both NB and HBO (**Figure 1**, TR = 3 s). There were no statistical differences in either BOLD and CBF percent changes between the NB and HBO conditions.

To evaluate the possible contribution of inflow effect, experiments were also performed with 10 s TR (**Figure 2**). The BOLD response with 10 s TR was not statistically different from that with 3 s TR. This result indicates that inflow effects did not significantly contribute (0.5% of the 3% change) to the observed BOLD fMRI response under HBO. The variable TE experiments showed that the BOLD change when extrapolated to TE = 0 was close to zero (**Figure 3**). This result indicated that spin-density effects at the given TE did not significantly contribute to the BOLD fMRI response under HBO.

Figure 2.



To determine whether the BOLD fMRI signal was saturated at 3 ATA HBO, T_2^*-weighted signal at NB, normobaric oxygen, and at 2 and 3 ATA HBO was acquired (**Figure 4**). T_2^*-weighted signals from the S1 and SSS showed strong dependence on increasing inhaled [O_2], with the signal changes being markedly larger in the SSS compared to S1. The image contrast between SSS and surrounding brain tissue decreased with increasing inhaled [O_2]. The T_2^*-weighted signals of the cortex and especially the SSS were still increasing up to 3ATA HBO.

To evaluate the possible contribution of differences in neural activity, electrophysiolgoical experiments under baseline and stimulated conditions were performed (**Figure 5A**). Under baseline conditions, spontaneous electrical activity was overall slightly lower under HBO compared to NB. Analysis of different frequency bands of the spontanesous electrical activity showed that spontaneous activities of the theta, alpha, beta and gamma bands were statistically different between HBO and NB, but not the delta band. Under stimulated conditions, electrical activity measured by local field potential was significantly lower under HBO compared to NB (**Figure 5B**).

CONCLUSION fMRI under HBO offers a means to evaluate the role of oxygen in neurovascular coupling as well as the effects of oxygen on basal and evoked BOLD and CBF signals. Our data support the hypothesis that activation-induced CBF regulation in the brain does not operate through an oxygen-sensing mechanism and that stimulus-evoked BOLD responses and venous T_2^*-weighted MRI signals still have room to increase under 3ATA HBO. fMRI and electrophysiological measurements under HBO, provide insights into the effects of HBO on neural activity, neurovascular coupling, tissue oxygenation, and BOLD fMRI signals.

REFERENCES. 1) Muir et al. *MRM* 2014. 2) Sicard et al. *Neuroimage* 2005. 3) Mulkey et al. *J Appl Physiol* 2004.

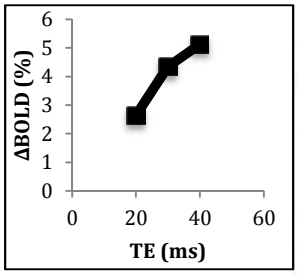


Figure 3

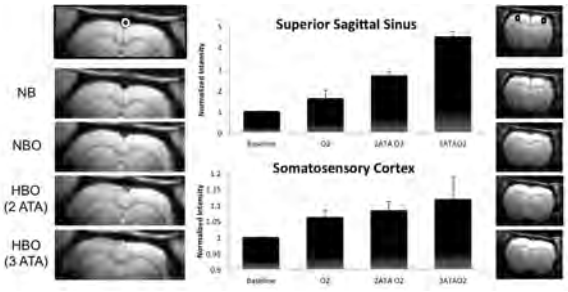


Figure 4

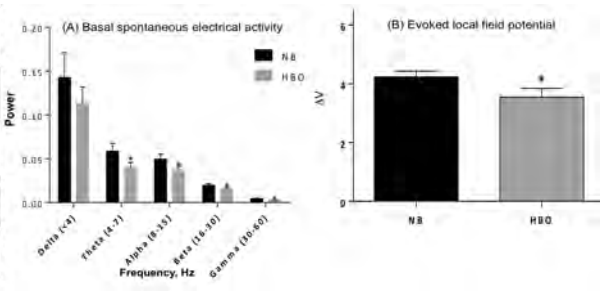


Figure 5