BOLD Evoked Response during Hyperbaric conditions

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

PURPOSE. Metabolism and blood flow are tightly coupled to neural activity. The most popular fMRI technique by far is based on the blood oxygenation level dependent (BOLD) signal. There are substantial interests in the effects of basal oxygen saturation on BOLD fMRI responses. In this study, we evaluated BOLD responses to forepaw stimulation in rats under i) normobaric air (NB), ii) normobaric oxygen (NBO), iii) hyperbaric air (HB), and iv) hyperbaric oxygen (HBO). Our central hypothesis was that BOLD % change is negligible under HBO because blood hemoglobin is already completely saturated.

METHODS. A custom-made hyperbaric chamber was constructed for use in the MRI scanner[1]. Male SD rats (n=9, 325±50g) were anesthetized with a bolus of α-chloralose at 60mg/kg iv and a 30mg/kg/hr infusion 30 minutes later. The rats were imaged 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] The rat was provided a separate gas-line within the chamber that allowed either air or 100% O_2 to be inhaled by the animal. Measurements were made during: i) normobaric air, ii) normobaric oxygen, iii) 3 atmospheres absolute (ATA) hyperbaric air, and iv) 3ATA hyperbaric oxygen.

Gradient-echo BOLD fMRI was acquired at 7T using a 2cm brain surface coil with FOV=25.6x25.6x30mm, matrix=96x96, TE=20ms, TR=3s, and seven 1.5mm thick slices. Regions of interest (ROIs) in the S1 region were used to find percent changes between stimulation and resting periods. Evoked BOLD changes in response to forepaw stimulation were calculated.[2] Statistical analysis was completed using paired t-tests with bonferroni-holm correction.

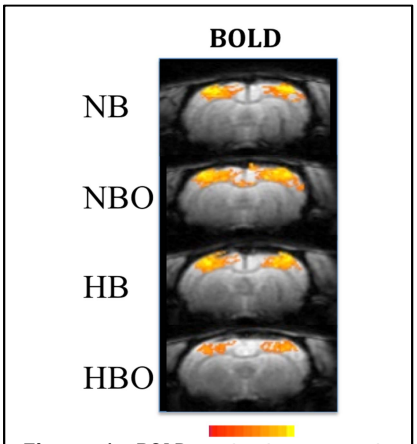

Figure 1. BOLD activation maps in response to forepaw stimulation. Averaged across subjects (n = 9). Color bar indicates 1-7% changes.

RESULTS. SpO_2 increased significantly from 95% at NB to 99% at HBO as expected. Respiration rate decreased significantly from 78 at NB to 56 bpm at HBO. Heart rate didn't change significantly with increasing inhaled O_2 concentration (P>0.05). Forepaw stimulation evoked reproducible activations in BOLD fMRI in the bilateral primary somatosensory cortices under the 4 experimental conditions (Figure 1). Group data shows that the HB conditions are significantly different from both the NB and NBO conditions (Figure 2).

DISCUSSION. Contrary to our hypothesis, robust and strong stimulus-evoked BOLD responses were detected under HBO, indicating BOLD responses are independent of inhaled [O_2]. Potential explanations are that: i) blood hemoglobin is not completely saturated under HBO and there is room for BOLD to increase by stimulation or in-flow effect, which is likely small if present.

An unexpected result is the significant increase in evoked BOLD response at the HB condition compared to both NB and NBO. This could be incited by increased or irregular neural activity at high pressures, as has been observed in vitro[3].

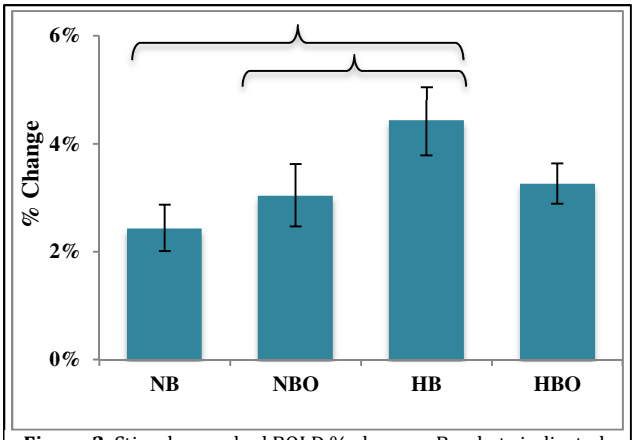

Figure 2. Stimulus-evoked BOLD % changes. Brackets indicated statistical significance.

CONCLUSION. fMRI under hyperbaric conditions offers a means to evaluate the effects of hyperbaric pressure and basal oxygen saturation on BOLD fMRI responses and on the role of O_2 in neurovascular coupling. We found that stimulus-evoked BOLD responses still have room to increase under HBO, indicating that full saturation might not have occured. Further investigations are needed to exclude other possible explanations. Future studies will include obtaining basal and evoked electrical activity under HB and HBO conditions. Since NBO and HBO are commonly used to treat a number of diseases, improved understanding of the effects of pressure, tissue oxygenation and blood flow, as well as evoked responses under NBO, HB and HBO, have potential clinical implications.

REFERENCES. 1) Muir et al. *MRM* 2013 (in press). 2) Sicard et al. *Neuroimage* 2005; 25:850. 3) Mulkey et al. *J Appl Physiol* 95:922-930.