

## SYNOPSIS

▪ Cerebrovascular responses during the inhalation of oxygen (100% O<sub>2</sub>) and carbon dioxide (5% CO<sub>2</sub>) in normal brain tissue are important for investigating exogenous regulation of cerebral hemodynamics. Although there have been numerous attempts to characterize varying aspects of vascular responses to O<sub>2</sub> and CO<sub>2</sub>, to our knowledge, there has not been comprehensive investigation of cerebrovascular activity by multi-parametric MRI techniques.

▪ In this study, we characterized various cerebrovascular parameters in response to 100% O<sub>2</sub> and 5% CO<sub>2</sub> gas inhalation using multiple MRI techniques in rat models. In particular, using both gradient and spin echo echo planar imaging (GE-EPI and SE-EPI) pulse sequences, we quantified blood oxygenation level dependence (BOLD), cerebral blood flow (CBF), and blood volume (CBV) changes with arterial spin labeling and an intravascular contrast agent.

## METHOD

▪ We characterized gas-induced vascular changes of anesthetized healthy rat brains (n=6, 1.5% isoflurane, mechanical ventilation) using MRI during 100% O<sub>2</sub> and 5% CO<sub>2</sub>.

▪ Arterial spin labeling (ASL), GE- and SE-EPI, and an intravascular superparamagnetic contrast agent (MION) were used to quantify vascular responses in blood oxygenation level dependence (BOLD), cerebral blood flow (CBF) and cerebral blood volume (CBV:  $\Delta R_2^*$ ), microvascular volume (MVV:  $\Delta R_2$ ), and vessel size index (VSI =  $\Delta R_2^* / \Delta R_2$ ) from various brain regions.<sup>1,2</sup>

▪ Each MRI run was consisted of a 5 min baseline (air) acquisition followed by 10 min 100% O<sub>2</sub> or 5% CO<sub>2</sub> inhalation and another 5 min baseline acquisitions.

▪ Various fMRI activation maps based on vascular responses to gas stimuli were created by a voxel by voxel t-test between the on and off stimulus periods.

## RESULTS

▪ Inhalation of 100% O<sub>2</sub> resulted in statistically significant increases of BOLD-weighted MRI signal ( $p < 0.01$ ) and significant decreases of CBF and CBV ( $p < 0.05$ ) in various brain regions (e.g., Fig.1). Despite the decreasing trend, no statistically significant change was observed either in MVV or in VSI.

▪ During 5% CO<sub>2</sub> challenges, BOLD signal, CBF, and CBV measured from the identical regions were all significantly increased ( $p < 0.05$ ), independent of echo type. However, no statistically significant increase was observed in VSI despite the increasing trend, which suggests vasodilation.

▪ Using the Grubb's expression:  $1 + \Delta CBF = (1 + \Delta CBV)^{\alpha}$  and GE pulse sequence, average  $\alpha$  calculated to be  $4.08 \pm 1.33$  and  $2.48 \pm 0.73$  in cortex during hyperoxia and hypercapnia, respectively ( $4.01 \pm 1.37$  and  $2.53 \pm 0.62$  using SE).

▪ Difference between BOLD functional activation maps acquired using O<sub>2</sub> and CO<sub>2</sub> as stimuli was evident, indicating caudate regions of brain differently responded to two gases (Fig. 2). Such anatomical differentiations of response magnitude were also manifest for other imaging parameters (i.e., CBV and CBF).

## DISCUSSION

We have demonstrated that neurovascular responses to 100% O<sub>2</sub> and 5% CO<sub>2</sub> inhalation are inherently different in terms of response magnitude and spatial distribution. O<sub>2</sub> inhalation resulted in increases of BOLD-weighted MRI signal and decreases in CBF and CBV while CO<sub>2</sub> resulted in increases of BOLD, CBF and CBV. O<sub>2</sub>-induced changes of vascular parameters were greater in subcortex than those quantified in other brain regions. Functional activation maps acquired using O<sub>2</sub> and CO<sub>2</sub> were different.

## CONCLUSION

Our results strongly suggest that gas-dependent cerebral blood supply is regulated by different biophysical mechanisms and/or affected by changes in overall baseline physiology induced by exogenous inhalants.

## ACKNOWLEDGEMENT

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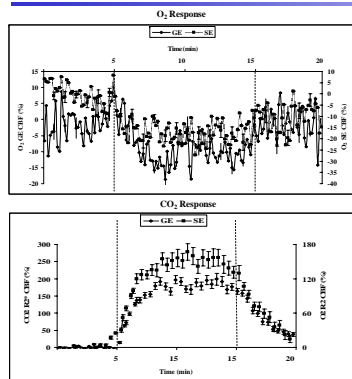


Figure 1. Representative CBF responses of cortex during O<sub>2</sub> and CO<sub>2</sub> inhalation, arrows indicating the onset of gas change.

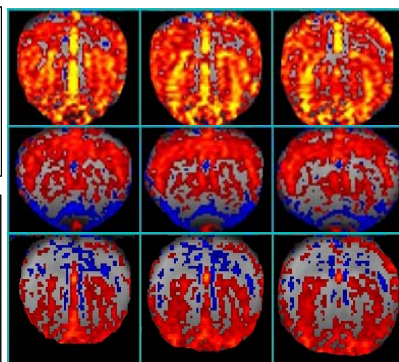


Figure 2. Functional activation maps using BOLD-GE-O<sub>2</sub> (first row), BOLD-GE-CO<sub>2</sub> (second row), and the difference (third row).