Effects of Oxygen and Carbon Dioxide on BOLD, CBF, CBV and VSI in anesthetized rats

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ABSTRACT Cerebrovascular responses during the inhalation of oxygen (100% O_2) and carbon dioxide (5% CO_2) 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_2 and CO_2, to our knowledge, there has not been comprehensive investigation of cerebrovascular activity by multi-parametric MRI techniques, providing both spatial and temporal information. In this study, we characterized various cerebrovascular parameters in response to 100% O_2 and 5% CO_2 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 the use of arterial spin labeling and an intravascular contrast agent.

MATERIALS AND METHODS We characterized gas-induced vascular changes of anesthetized healthy rat brains (n=6, 1.5% isoflurane, mechanical ventilation) using magnetic resonance imaging (MRI) during 100% O_2 and 5% CO_2. 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: $\Delta R2^*$), microvascular volume (MVV: $\Delta R2$), and vessel size index (VSI = $\Delta R2^*/\Delta R2$) from various brain regions.[1,2] Each MRI run was consisted of a 5 min baseline (air) acquisition followed by 10 min 100% O_2 or 5% CO_2 inhalation and another 5 min baseline acquisitions. Using the Grubb's expression: $1+\Delta CBF = (1+\Delta CBV)^{\alpha}$, we calculated the relationship between CBF and CBV changes. Arterial blood pressure, oxygen saturation level, body temperature, and heart rate were monitored throughout the experiment. Additionally, 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 AND DISCUSSION Inhalation of 100% O_2 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 ($p>0.05$). During 5% CO_2 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 gradient echo (GE) pulse sequence, average αcalculated to be 4.08±1.33 and 2.48±0.73 in cortex during hyperoxia and hypercapnia, respectively (4.01±1.37 and 2.53±0.62 using spin echo (SE)). The mean arterial pressure was also drastically affected by hyperoxia and hypercapnia (108.26±18.19 and 81.15±26.26 mmHg, respectively baseline 99.16±24.95 mmHg). On the other hand, a disparity between BOLD functional activation maps acquired using O_2 and CO_2 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). We have demonstrated that multiple vascular parameters such as BOLD, CBF, CBV, and VSI changes can be used for studying the mechanisms that regulate cerebral perfusion and oxygenation for providing insights into the recovery mechanisms of O_2-treated stroke animal models. Our results strongly suggest that gas-dependent cerebral blood supply is regulated by different biophysical mechanisms and/or may affected by changes in overall baseline physiology (i.e., blood pressure) induced by exogenous inhalants.

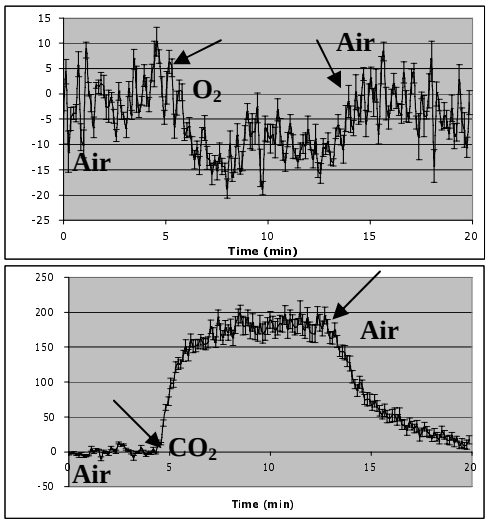

Figure 1. Representative CBF responses during O_2 and CO_2 inhalation, arrows indicating the onset of gas change.

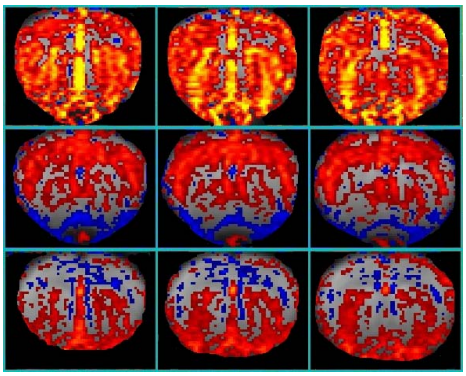

Figure 2. Functional activation maps using BOLD-GE-O2 (first row), BOLD-GE-CO2 (second row), and the difference (third row)

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