Evaluation of cerebral energy demand during graded hypercapnia

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ABSTRACT The cerebral metabolic rate of oxygen ($CMRO_2$) is a physiological parameter closely linked to neural activation as well as to various disease states. Hypercapnic calibration is used to calibrate the BOLD-CBF-CBV relationship under the assumption of iso-metabolic blood flow increase during CO_2 inhalation [1]. At the same time, simultaneous measurements of cerebral blood volume (CBV), hemoglobin oxygen saturation (SO_2) and blood flow (CBF) necessary to calculate $CMRO_2$ changes can be obtained non-invasively using near infrared optical spectroscopy with the caveat of reduced spatial resolution and depth sensitivity. In this study we used optical measurements obtained during graded hypercapnia (2.5-5-7.5% CO_2, Fig. 2) to test the iso-metabolic assumption, and demonstrated an apparent increase in brain metabolism at higher inhaled CO_2 levels.

MATERIALS AND METHODS Four normal healthy Sprague-Dawley rats (~300g) were used to record hemodynamic parameters during stepped CO_2 breathing gas changes. A combined optical/MR probe assembly (Figure 1) was fabricated to fit in the animal holder of a small-bore 9.4T MRI system (Bruker). In this submission, we only report the results from the optical measurements. The optical system consisted of a frequency domain spectrometer (FD-NIRS) that provided absolute optical properties at 7 near-infrared wavelengths between 670 and 830 nm at 12.5 Hz [2] and a diffuse correlation spectrometer (DCS) that provided the time-resolved temporal auto-correlation of the diffusely reflected light at ~1 Hz [3,4]. Hemoglobin concentration and oxygenation were calculated by fitting the optical absorption coefficient at the 7 wavelengths to the known oxy and deoxy-hemoglobin spectra and a correlation diffusion model was used to extract a blood flow index from the temporal auto-correlation functions. Both optical measures were obtained at 4 probing depths, determined by the distance between the source and detection optical fibers (5,8,11,14 mm, respectively). An average of all distances was used for subsequent $CMRO_2$ computation. The relative $CMRO_2$ during gas changes compared to baseline was calculated as $rCMRO_2=rCBF.rCBV.rOEF$, where rCBF was measured directly with the DCS instrument, rCBV was obtained from rHbT (the ratio of total hemoglobin concentration) and $rOEF=(S_{a,O2}-SO_{2final})/(S_{a,O2}-SO_{2initial})$, with $S_{a,O2}$ the arterial hemoglobin oxygen saturation, SO_2 the tissue averaged hemoglobin saturation.

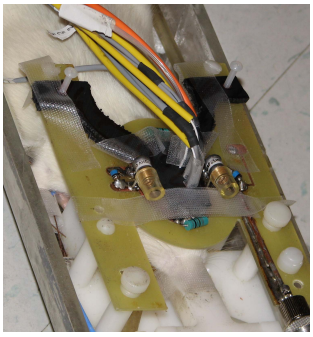

Fig. 1. Optical-MR probe

RESULTS AND DISCUSSION Figure 3 shows sample time-traces of optical total hemoglobin (HbT), tissue hemoglobin saturation (SO_2), cerebral blood flow (CBF) and $CMRO_2$ during stepped increases from 0 to 2.5% (cyan highlight), 5% (green) and 7.5% (red) respectively of the amount of CO_2 in the breathing gases. Progressive increases in both CBV and CBF are noted, with a simultaneous decrease in the oxygen extraction fraction. Initial results appear to indicate increased $CMRO_2$ during the hypercapnic episodes (Fig .4). Further investigation is warranted.

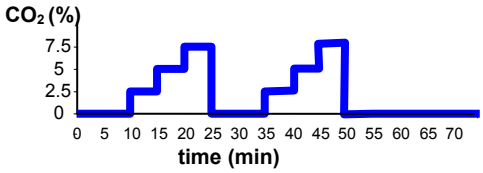

Fig. 2. Protocol

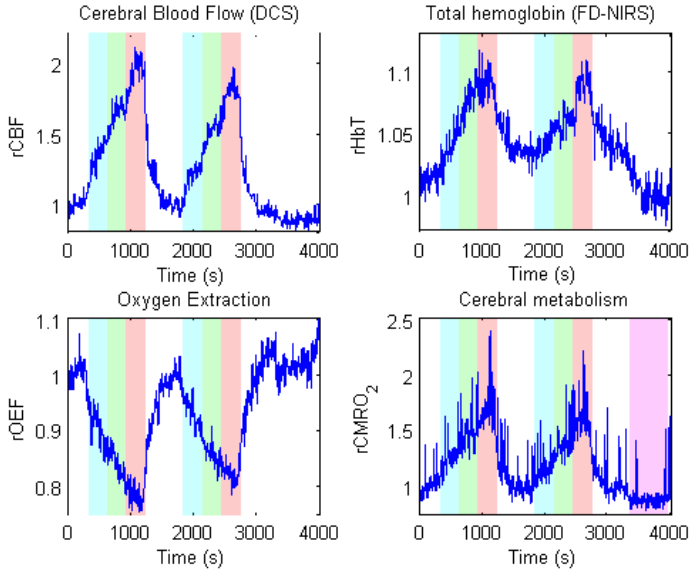

Fig. 3. Example blood flow, volume, Hb saturation and metabolism.

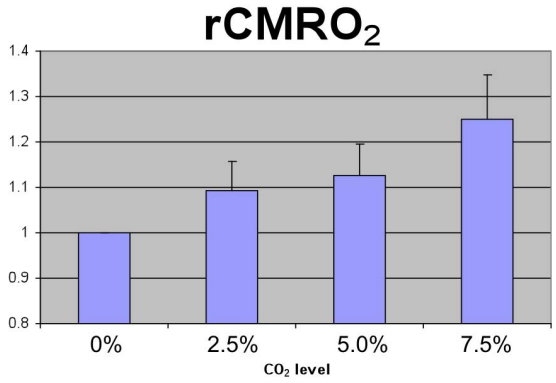

Fig.4 Relative metabolism from all animals

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