Measuring Cerebral Metabolism of Oxygen with multimodal MRI and Near-infrared Spectroscopy

Q. Zhang[1,2], Y. Wu[2,3], U. Tuor[2,4], D. Kirk[2,3], F. Tadeusz[4], K. Deka[3], M. Smith[1,5], and J. Dunn[2,3]

[1]Electrical and Computer Engineering, University of Calgary, Calgary, AB, Canada, [2]Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada,

[3]Experimental imaging center, Foothills Medical Center, [4]Institute of Biodiagnostics-west, National Research Council, [5]Radiology, University of Calgary

Introduction

Cerebral metabolic rate of oxygen (CMRO2) is the measurement of O2 which is consumed in the brain by metabolic processes and is an important indicator of brain function. A non-invasive means of accurately measuring CMRO2 would provide an important tool for exploring the cerebral pathophysiology. Based on Fick's equation, CMRO2 can be derived from the product of cerebral blood flow (CBF) and arteriovenous O2 difference (AVO2), parameters which may be obtainable through a multimodality MR and near-infrared spectroscopy (NIRS) system.

In the present study, a novel method for measuring CMRO2 was implemented. We used CBF measurements – obtained with MRI arterial spin labeling (ASL) – combined with measurements of cerebral deoxy-hemoglobin and total hemoglobin concentration – measured using a broadband NIRS system, to determine CMRO2. The CMRO2 is temperature-dependent [1]. To validate this method, the combined MRI/NIR system was used to measure CMRO2 following hypothermia in a rat model.

Materials and Methods

Animal preparation: Wistar rats (n = 7) were anesthetized with 2.5% isoflurane in oxygen (0.3 l/min) and nitrogen (0.7 l/min) administered by means of a face mask. The femoral artery was cannulated for blood gas measurements. Rectal temperature was monitored and temperatures adjusted with a controlled water pad. The hair of rat at the top of the head was removed from the scalp, and a pair of optodes 7mm apart were fixed to the head for NIRS.

Hypothermia experiment: The temperature was first maintained at 37±0.5°C for normothermia, and was decreased to 33±0.5°C for hypothermia.

MR imaging acquisition: Imaging was performed using a 9.4T horizontal bore (21 cm) magnet (Magnex, UK) equipped with an Advance console (Bruker, Germany) and a 5cm quadrature birdcage coil. Perfusion images and T1 maps were acquired at normothermia and hypothermia respectively. A series of 12 inversion-recovery *T*1-weighted Snapshot-FLASH images were required with TE=1.8ms and 12 inversion delays. Perfusion imaging was to measure CBF using single coil arterial spin labeling, TR=3.55ms, TE=2.1ms, flip angle=12 [2]. The RF pulse for arterial labeling was an adiabatic inversion pulse 3 s long in the presence of a 1.5G/cm field gradient followed by a Turbo FLASH imaging sequence. Two pairs of proton density images with inversion labeling and controls were acquired.

Hemoglobin measurement: A home-constructed NIRS system, based on Andor spectrograph and CCD camera (Andor, Northern Ireland), was used to measure the concentration of hemoglobin simultaneously with MRI acquisition. The NIRS system directly measured the concentration of deoxy-hemoglobin in cerebral tissue using the second differential method [3], and determined the total hemoglobin in cerebral tissue using 55s anoxia pulse. Combined with the hemodynamic parameter in artery, obtained from blood gas, the AVDO2 would be derived [4].

Data analysis: The MR images were processed using Marevisi (National Research Council, Canada). The CMRO2 was derived from the product of CBF and AVDO2. Measurements of CBF and CMRO2 were made within the detected regions of NIRS system in the rat brain cortex. The values were presented as the mean±SD. A paired *t*-test was used to compare normothermia-hypothermia difference. Differences were significant if $p<0.05$.

Result and Discussion

CBF (Fig. 1) declined with hypothermia (Fig. 2a). The CBF was 118±26ml/100g/min (mean±SD) at normothermia and 94±11ml/100g/min at hypothermia. Although two animals showed major declines in CBF, the average change was not significant change in CBF ($p=0.15$). Brain mean cerebral oxygen saturation (SmcO2) was almost constant (within 5% range) and changed from 71.28±2.37% at normothermia to 73.39±1.29% at hypothermia (Fig. 2b). The CMRO2 declined significantly from 2.84±0.71μmol/g/min at normothermia to 1.91±0.07μmol/g/min at hypothermia. ($p=0.03$) (Fig. 2c).

The results demonstrated that the MRI/NIR multimodality method could be used to measure CMRO2 and changes in CMRO2. The variability in the individual responses may relate to the anesthesia, but showed additional merit of the multimodality system in those subjects with large changes in CBF tended to have little change in saturation—i.e. there was individual variation in response. The temperature-dependence in CBF and CMRO2 in the hypothermia experiment was similar to that previously reported [1, 5]. Hypothermia tended to produce reductions in CBF and CMRO2, but the significant difference between normothermia and hypothermia in CMRO2 indicates that CMRO2 has a stronger temperature-dependence than CBF.

References

1. Hagerdal, M., et al., Journal of Neurochemistry, 1975. **24**: p. 311-316.
2. Lei, H., et al., Brain Research, 2001. **913**: p. 174-9.
3. Matcher, S.J., et al., Phys Med Biol, 1994. **39**(1): p. 177-96.
4. Kaminogo, M., et al., Stroke, 1995. **26**(12): p. 2358-60.
5. Klementavicius, R., et al., 1996. **85**: p. 482-487

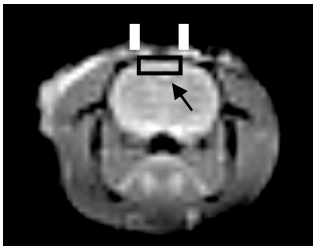

Figure 1. perfusion image. Approximate optodes positions are indicated by white bars. Black square indicates ROI for perfusion and CBF data. Arrow indicates lower (darker) perfusion in corpus callosum white matter.

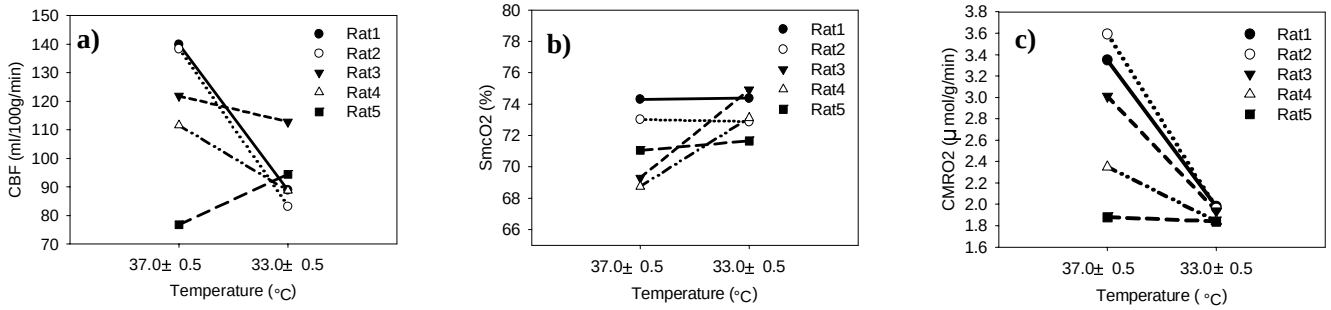

Figure 2. Physiological changes from normothermia (37±0.5°C) to hypothermia conditions (33±0.5°C). Each individual is plotted as one line. a) CBF; b) CBV; c) CMRO2.