Multimodal MRI and NIRS Measurement of CMRO2 in Grey Matter

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Target audience: Those using MRI to study metabolic rate and oxygenation in humans and animal brain.

Purpose: To determine the reliability of a method of quantifying cerebral metabolic rate for oxygen ($CMRO_2$) by combining MRI and near infrared spectroscopy (NIRS). We hypothesize that controlled hypothermia applied to rats will reduce their $CMRO_2$ and our human $CMRO_2$ measured using this method will be comparable to literature value.

Methods: The animal experiments consisted of Wistar rats (n=7), which were anesthetized with 2.5% isofluorane in 0.3 L/min of oxygen with a face mask. The femoral artery was cannulated for blood gas measurements. Rectal temperature was maintained at 37.0 ± 0.5 °C for normothermia, and was decreased, using a cold water pad, to 33 ± 0.5°C for controlled hypothermia. MRI and NIRS data were collected for both conditions. MR Imaging was performed using a 9.4-T Bruker Avance II console and a 5cm quadrature birdcage coil. A series of 12 inversion-recovery *T*1-weighted Snapshot-FLASH images were required with TE=1.8ms and 12 inversion delays. CBF was measured using single coil arterial spin labeling, TR=3.55ms, TE=2.1ms, flip angle=12. The RF pulse for arterial labeling was a flow driven adiabatic inversion pulse 3 s long in the presence of a 1.5-G/cm field gradient followed by a Turbo FLASH imaging sequence. Two pairs of proton density images with inversion labeling and controls were acquired. The NIRS system is custom built with an Andor imaging spectrograph and a charge-coupled device camera (Shamrock 303i, Andor Technology Inc, Northern Ireland). 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 measurements. Deoxyhemoglobin concentration was obtained using a second differential method. Total hemoglobin and subsequently tissue oxygenation was measured and calculated by applying 50s of anoxia pulse[1]. Combined with the CBF data from MRI, we used the Fick equation[2] to calculate $CMRO_2$: $CMRO_2$ = CBF x ($S_aO_2 - S_vO_2$) x [tHb] x O_2 carrying capacity, where S_aO_2 is the arterial oxygenation, S_vO_2 is the venous oxygenation, which can be calculated by NIRS[3]. tHb can be determined by the blood sample, and O_2 carrying capacity at an assumed value. The human study consisted of control subjects (n=9), and imaging acquisition was repeated on 2 subjects 6 month apart for a total of 11 data sets. MR imaging was performed using a 3T GE Discovery MR750 and a 12-channel head coil. CBF was measured using a pseudo-continuous arterial spin labeling[4] (TR=4813 ms, TE=11.1 ms, post label delay=1500ms). The NIRS data was collected using a frequency domain system (ISS), which was capable of quantifying hemoglobin concentrations. The arterial oxygenation was measured using a pulse oximeter, and large vessel hemoglobin concentration was assumed to be 15g/dL.

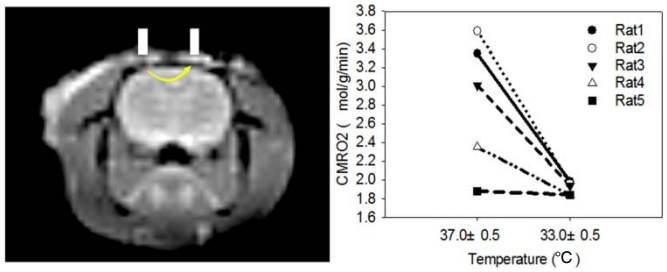

Fig 1. Animal perfusion image from ASL. Approximate optodes positions are indicated by white bars. Yellow arrow indicates ROI for perfusion and CBF data.

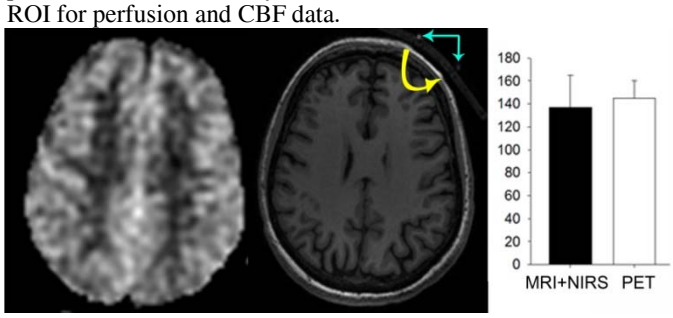

Fig 2. Human perfusion image from ASL (left); area of NIRS measurement is indicated by the yellow arrow. Anatomical images are used to find location of the probe marked by Vitamin E capsules, indicated by the teal arrow (middle). There is good agreement between the $CMRO_2$ calculated using this method and the PET (see results) values (Right). The values are presented as mean± SD

Results: Rat $CMRO_2$ (Fig 1) at normothermia was 2.84±0.84 umol/g/min and declined to 1.91±0.07 umol/g/min under the hypothermia condition (p=0.03). There were no significant differences in the CBF or micro-vascular saturation for the two temperatures. The average frontal cortex $CMRO_2$ (Fig 2) in the human control subjects is 137 ± 28 umol/100g/min, with an average CBF of 60 ± 10 mL/100g/min and microvascular saturation of 63±5%. For comparison, $CMRO_2$ measured using PET was similar at 145 ± 15 umol/100g/min [5, 6, 7]. The light path in patients contains proportionately more non-brain (i.e skull and CSF) than in animals which has led to the suggestion that NIRS cannot be used to quantify $CMRO_2$ in humans[8] (Figs 1, 2), It is possible that measuring changes in human brain may be more accurate than measuring absolute values.

Conclusion: The results of the animal experiment demonstrated that the MRI/NIRS method could be used to measure and detect changes in $CMRO_2$. The $CMRO_2$ control subjects obtained using MRI/NIRS method is in good agreement with the $CMRO_2$ reported the average value of several PET studies. This suggests that multimodal MRI/NIRS can measure absolute or changes in $CMRO_2$.

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