Mapping of Cerebral Oxidative Metabolism in Concussion Patients

Xiang He[1], Serter Gumus[2], Hoi-Chung Leung[3], Parsey Ramin[4], Mark Schweitzer[1], Marion Hughes[2], Lea Alhilali[2], and Saeed Fakhran[2]

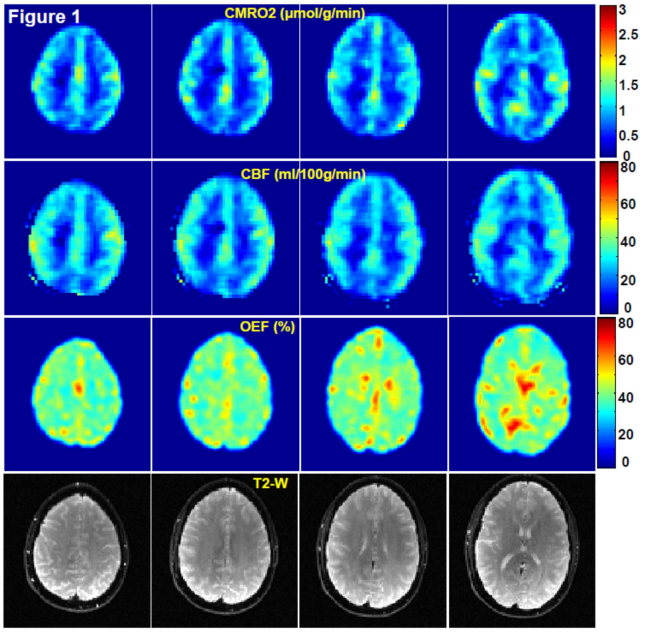
[1]Department of Radiology, Stony Brook University, Stony Brook, New York, United States, [2]Department of Radiology, University of Pittsburgh Medical Center, pennsylvania, United States, [3]Department of Psychology, Stony Brook University, New York, United States, [4]Department of Psychiatry, Stony Brook University, New York, United States

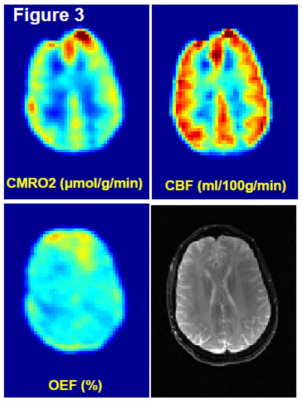
Introduction: Concussion, or mild TBI (mTBI), normally does not involve structural damage to brain tissue or blood vessels. It has been essentially viewed as a metabolic problem (1,2). After initial period of hyperglycolosis coupled with reduced cerebral blood flow, the concussed brain goes into a diffuse prolonged depression of metabolism with continued neurometabolic cascade, which may result in impaired mitochondrial function (3,4). The post-concussion glucose hypo-metabolism, which occurs both globally and regionally, has been correlated with attention deficits, increased irritability, social withdrawal, sleep and memory problems, and depression. While oxidative stress plays an significant role in the pathophysiology of mTBI, only a few research has been devoted to study the brain oxidative metabolism (5). This study constitutes one of the first MRI-based approaches to investigate the regional cerebral oxidative metabolism (CMRO2) and oxidative stress in post-concussion patients.

Multi-slice quantitative BOLD (qBOLD) technique has been developed and validated to evaluate brain hemodynamic parameters, i.e. oxygen extraction fraction (OEF) and deoxygenated blood volume in the baseline state (6,7) and during neuronal activation (8). By combing with the mapping of CBF using ASL, it becomes feasible to non-invasively estimate regional CMRO2 across the whole brain.

Methods: All experiments were performed on 3T Siemens Trio scanners using either 32-channel or 12-channel head RF coil. 9 subjects (5 healthy volunteers and 4 post-concussion patients) were recruited in this IRB-approved study. MRI parameters for 2D qBOLD data were: FOV of 256x256 mm^2; voxel size of 2x2x4 mm^3; 4-5 interleaved slices with 100% spacing; TR of 1000 ms; 4 repetitions with total acquisition time of ~8 minutes. Navigator echoes were inserted to evaluate the B0 drifting. Pseudo-continuous ASL (pCASL) with background suppression and segmented echo-shifting 3D-GRASE acquisition was implemented (7). Total labeling time was 1600ms with a post-labeling delay of 1400ms. Other parameters were: voxel size of 4x4x4 mm^3; matrix of 64×48×28; 2_{PAR}× 2_{PE} segmentation; echo spacing of 700μs and echo train duration of 21 ms; refocusing RF flip angle of 120°; TR of 4 sec with total acquisition time of ~7 min (12 label/control pairs).

Results & Discussions: The MR qBOLD data was processed individually before the estimated maps were averaged. CBF were calculated using the standard approach. CMRO2 was subsequently calculated as the product of CBF and OEF. Figure 1 shows the estimated maps of CMRO2 (μmol/g/min), CBF (ml/100g/min) and OEF(%) acquired at four slices from a concussion patient. Notice the artificially high OEF values around ventricles, which are caused by un-accounted decay from field inhomogeneities. They normally don't create noticeable artifacts in the CMRO2 map due to very low perfusion in deep WM region. All concussion patients demonstrated a reduced oxidative metabolism, except for one patient which showed abnormally higher oxidative metabolism, as illustrated in Fig. 3 (mean CMRO2/CBE/OEF of 1.93 μmol/g/min, 61.5 ml/100g/min and 35.4%). This patient suffers from multiple post-traumatic seizures, which is known to increase both blood flow and oxygen metabolism(9). Excluding this concussion patient with seizure, the mean GM CMRO2 in concussion patient is 1.03± 0.15 μmol/g/min, mean GM CBF is 33.8± 5.1 ml/100g/min.





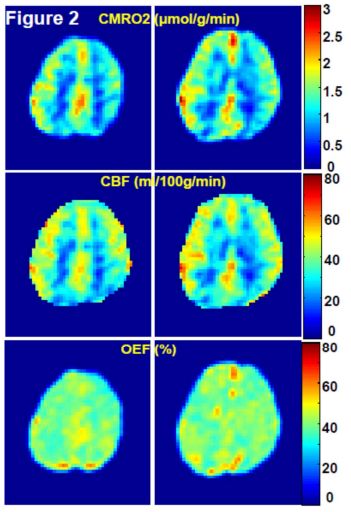


Figure 2 presents CBF and CMRO2 maps from a healthy control subject. Averaged across five control, the mean GM CMRO2 is 1.46 ±0.17 μmol/g/min, mean GM CBF is 45.6 ±8.1 ml/100g/min. Therefore, concussion patients feature a depressed CMRO2 and CBF, which is consistent with PET findings from animal concussion model (10) a patient study using arteriovenous oxygen difference (5). Based on the limited data in this study, no significant OEF difference has been observed (38.1 ±2.8% in control vs 34.9± 1.7% in patient), suggesting that the observed oxidative hypo-metabolism is mainly due to the reduced blood perfusion (5). This is also consistent with the notion of mitochondrial related impairment.

Conclusion: By combining MR-qBOLD and pCASL technique, this study demonstrated the feasibility of non-invasively mapping whole oxidative metabolism on concussion patients. Depressed gray matter CMRO2 (-29%) and CBF (-26%) has been observed in post-concussion patients. Hence, the proposed technique provides a potential tool to non-invasively monitor the brain metabolic response in mTBI without radiation, which is especially important to study sports-related concussion in adolescent and young patients.

References: **(1)** Tavazzi, et al, Neurosurgery 2007;61:p390. **(2)** Vagnozzi, et al, Neurosurgery 2007; 61:p379. **(3)** Yoshino, et al, BrainRes 1991; 561:p106. **(4)** Aarsland, et al, JNeuroSci 2010; 289:p18. **(5)** Bouma, et al, J Neurosurg 1991;75:p685. **(6)** He, et al, MRM 2007; 57:p115. **(7)** He, et al, MRM 2008; 60:p882. **(8)** He, et al, ISMRM 2010;1119. **(9)** Meldrum, et al, Brain 1976: 99:p523. **(10)** Hovda, et al, BrainRes 1991;567:1.