EVALUATION OF THE BOLD SIGNAL IN RESPONSE TO CO2 OR O2 IN JIA PATIENTS AT 3T: A PILOT STUDY

Afsaneh Amirabadi[1], Adrian Crawley[2], Carina Man[1], Tammy Rayner[1], Ruth Weiss[1], Joseph Fisher[2,3], and Andrea Doria[1,4]

[1]The Hospital for Sick Children, Toronto, ON, Canada, [2]The University Health Network, ON, Canada, [3]Thornhill Research Inc., ON, Canada, [4]University of Toronto, ON, Canada

PURPOSE: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disorder of childhood, [1] with the knee being the most frequently affected joint. [2] Hypoxia is a common feature of the inflamed rheumatoid synovium [3] and plays a key role in the initiation and perpetuation of the inflammatory process. The objective of this study was to measure the JIA patients' knee joint vascular response to alteration of CO2 or O2 in comparison to the vascular response of healthy joints.

METHODS: The protocol was approved by our hospital Research Ethics Board. Eight JIA patients and 13 healthy controls participated in this study (median age, 16 years; range, 11–17 years). A facemask, secured around the subject's face, was attached to a sequential breathing circuit (RespirAct™, Thornhill Research Inc., Toronto, Canada). A 7-min functional BOLD EPI gradient echo sequence (TR/TE=2000/30 ms, flip angle=70°, matrix=64×64, slice thickness=5 mm) was acquired during the CO2/O2 manipulation for each subject. Stimulation was induced using the model-based prospective end-tidal (MPET) gas breathing sequences. [4] The sequencer precisely controlled the exhaled 'end-tidal' PETCO2 and PETO2 of expired gases while the BOLD signal was simultaneously recording. The subject baseline (B) O2 consumption and CO2 production were measured through a test run. The breathing protocol was divided into 6 segments as follow; for CO2 challenges: [B(1 min), B+5 mmHg(1min), B+10 mmHg(1min), B (2min), B-5 mmHg(1min), B(1 min)] while maintaining isoxia, and for O2 challenges: [B(1 min), B+30 mmHg(1min), B+80 mmHg(1min), B(2min), B-5 mmHg(1min), B(1 min)] while maintaining isocapnia. MRI acquisitions were conducted using a Siemens Trio Tim 3T system (Siemens, Erlangen, Germany) with 15 channel knee coil. A T1-weighted (TR/TE=673/20 ms, flip angle=150°, matrix=448×448, slice thickness=5 mm) scan was served as the anatomic reference for each subject. Percent signal change has been calculated from the region of interest manually-drawn around the synovium. Analyses were performed using the AFNI [5] software. Percent BOLD signal changes were reported as mean±standard deviation. Two sample student t-tests were performed to determine if there is any significance ($p<0.05$) signal change in response to stimuli between JIA and control subjects.

RESULTS: All subjects were able to finish both protocols, however they tolerated the O2 protocol better than the CO2 protocol. There were no significant differences in percent signal changes between arthritis (CO2: -0.17±0.33; O2: -0.11±0.34) and control (CO2: -0.03±0.43; O2: -0.12±0.35) groups in neither CO2 (P=0.60) nor O2 (P=0.91) challenges.

CONCLUSION/DISCUSSION: In this study, we used different steps of hypercapnia-hypocapnia and hyperoxia-hypoxia as a stimulus for BOLD studies of the knee joint. BOLD responses were detected in the synovium of all subjects from both groups. There was a substantial degree of variability in spatial location as well as in response amplitude along the synovium and among subjects. Results indicated that the mean BOLD signal changes in response to stimuli (CO2 or O2) were not significantly different between knees with active inflammation and control knees. In the previous study in our lab, [6] it was shown that 1.5T MRI signal to noise ratio was inadequate to indicate BOLD signal difference between knees with active inflammation and control knees. The study also suggested further investigation at higher field strength scanners. However, the current study indicated that an even higher field strength (3T BOLD MRI) was inadequate to show this difference. Further study with higher sample size is required to clarify this finding.

References:

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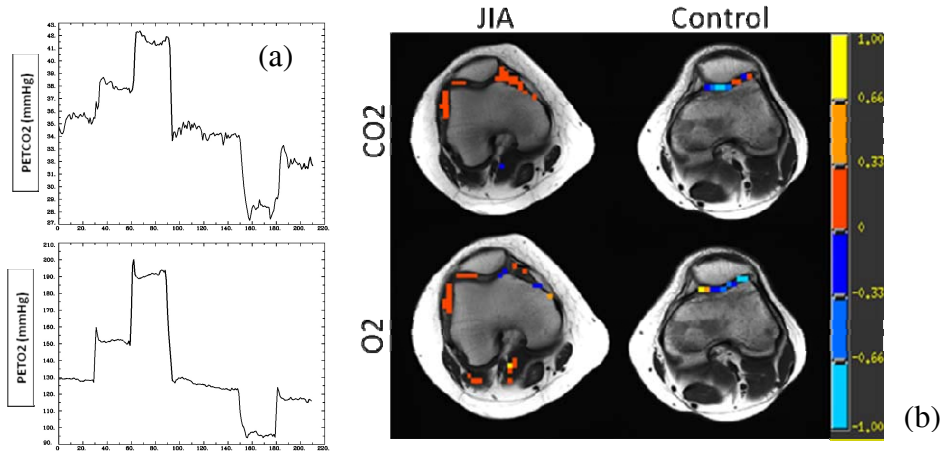

Fig1. (a) Time course of end tidal CO2 and O2, (b) BOLD activations in response to CO2 and O2 stimuli in arthritis and control knees' synovium superimposed on the anatomical images of representative subjects.