Measuring Human Brown Adipose Tissue Volume and Activity by Quantitative and Functional MRI

Jie Deng, PhD1,2; Lisa M. Neff, MD3, MS1,3; Richard Shore, MD1,2; Jonathan Samet, MD1,2; Christina Sammet, PhD1,2; Paige Nelson, BA2; Jennifer Lewandowski, MS, RD1; Karen Rychlik, MS2; Lewis Landsberg, MD1,3.

1Northwestern University Feinberg School of Medicine, Chicago, IL. 2Lurie Children’s Hospital, Department of Radiology, Chicago, IL. 3Northwestern Comprehensive Center on Obesity, Northwestern University Feinberg School of Medicine, Chicago, IL.

Background

- In the search for potential therapies for obesity and diabetes, brown adipose tissue (BAT) has emerged as a potential target of interest.
- In rodents, BAT is the tissue responsible for adaptive thermogenesis, or increased energy expenditure and heat generation during cold exposure and overfeeding.
- Emerging evidence suggests that BAT may play a role in glucose metabolism and insulin sensitivity. Potential mechanisms include: 1) acute increases in glucose and fatty acid utilization in metabolically active BAT deposits, 2) increased thermogenesis leading over time to changes in body composition, particularly decreases in body fat, and 3) paracrine or endocrine actions of adipokines secreted by BAT, such as interleukin-6 (IL-6) or fibroblast growth factor-21 (FGF-2).
- PET/CT after cold exposure is the current gold standard PET/CT will also be used as a control for the radiation exposure, and the inability to determine the composition of tissues that contain a mixture of brown and white adipocytes.
- Magnetic resonance imaging (MRI) is a non-ionizing radiation modality with superior spatial resolution and soft tissue contrast with which adipose tissues can be characterized and functionality.

Methods

Subjects: 15 lean (BMI 18.5–24.9) and 15 overweight/obese (BMI 25.0–50.0) male subjects, ages 18-24, will be recruited. Some inclusion criteria: Subjects must be within 3% of their maximal body weight and weight stable (+/- 3%) over the last three months. Some exclusion criteria: Thyroid conditions, diabetes, medications that might affect BAT activity, and implanted metal devices that might interfere with the MRI. Hypotheses:

1) BAT activation in response to cold exposure and overfeeding in BAT may play a role in glucose metabolism and insulin sensitivity.
2) Increased thermogenesis (NST), and after warm exposure, with increasing T2* in some regions but decreasing T2* in others.
3) Correlation of BAT volume and activity with glucose uptake in BAT detected by PET/CT.

Preliminary Results

- 15 lean subjects (BMI: 18.5 - 24.9 kg/m2) have completed the study. Data collection on overweight and obese volunteers is ongoing. Analysis of metabolic data (e.g. glucose, insulin) will be conducted at study conclusion.
- PET/CT scans for the completed lean subjects are shown in Figure 2. All 15 subjects had active BAT, but SUVmax (standard uptake value) varied widely (3.99 to 39.9 g/mL; mean 18.5 ± 10.9). The volume of metabolically active BAT also varied widely (3.1-189.3 mL; mean 100 ± 57.3 mL).
- MRI parameter changes were detectable at NST and WM, in comparison with the baseline TN condition. In this study, activation of BAT was detected on MRI scan by:
  1) Combustion of the fatty acids led to depletion of lipids within adipocytes and decreased unsaturated fatty acid synthesis. Decreased tissue fat percentage (PF) was observed in BAT at NST, likely due to fat depletion during BAT activation. Fatty acid double bond measurements ndb, nmdb, and chain length all tended to decrease after cold exposure (Figure 3).
  2) Oxygen consumption due to increased metabolism resulted in increased blood flow to provide oxygen supply to the tissue. With increased oxygen consumption, the level of deoxyhemoglobin in the blood increases resulting in decreased T2*. Increased blood flow can also bring in more oxygen and thus a decrease in regional deoxyhemoglobin and an increase in T2* (Figure 4). Overall, these changes significantly affected T2* (p = 0.037) (Figure 5).

Conclusions

- This study demonstrated that multi-parametric quantitative MRI images acquired under three thermal conditions provide multi-dimensional measurements for detecting BAT activation in lean subjects.
- These techniques can be exploited to investigate changes in BAT functionality in an obese population.
- Use of MRI techniques will enhance future studies targeting BAT activation and recruitment as a potential intervention for obesity and diabetes.

Figure 1. Imaging protocol.

Figure 2. Glucose uptake in BAT detected by PET imaging after cold exposure in 15 lean subjects.

Figure 3. MRI parameters prior to cold (TN), at non-shivering thermogenesis (NST), and after warm-up (WM). FF: fat percent; ndb: number of double bonds; nmdb: number of methyl interrupted double bonds; d: fatty acid chain length

Figure 4. Representative MRI scan showing changes in Fat Percent (FP) and T2* from baseline (TN), at non-shivering thermogenesis (NST), and after warm-up (WM).