



Water-Fat MRI Suggests an Endogenous Rhythm of Brown Adipose Tissue Proliferation in a Hibernator

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Introduction:

- Brown adipose tissue is the main thermogenic tissue in small eutherian mammals
- BAT is the main source of heat and increased metabolic rate during arousal from torpor in the 13-lined ground squirrel
- In non-hibernators BAT proliferation requires weeks of cold-acclimation

Research Questions:

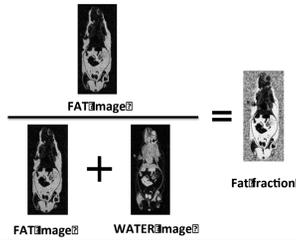
- **Question 1:** Does BAT proliferation occur seasonally in a hibernator *without* cold acclimation? Do both quantity and quality of BAT change?
 - Hibernator WAT varies with an endogenous circannual rhythm
- **Question 2:** Where does this BAT proliferation occur?

Imaging of BAT:

- Anaesthetized ground squirrels scanned at 3 Tesla with a 32 channel receiver array

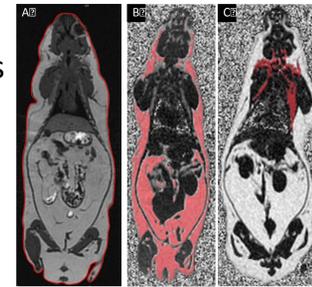
- Fat Fraction IDEAL [Water-Fat Image] (TR/ΔTE/flip angle = 8.0ms/0.97ms/1°, voxel dimensions = 0.9x0.9x0.9 mm³)
- T₁-weighted (TR/TE/flip angle = 4.3ms/2.0ms/15°, voxel dimensions = 0.9x0.9x0.9mm³)

- Distinguishes water from lipid allowing calculation of fat fraction



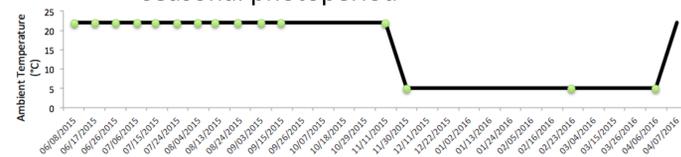
Segmenting Fat and Volume:

- Total squirrel volume manually segmented using T₁-weighted images (A). WAT volumes (red in B) segmented using Osirix 5.6 with parameters set to a lower Fat fraction threshold of 70%. BAT Fat fraction between 25 - 70% (red in C).

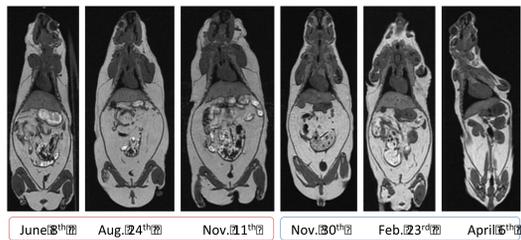


Experimental Timeline and conditions:

- 3 adults, 15 scans each over 11 months:
- June 6th – Nov. 11th animals held at 25°C, 1°C/day decrease to 5°C until April 6th
- seasonal photoperiod



White Adipose Tissue Volume



June 6th 2015, Aug. 24th 2015, Nov. 11th 2015, Nov. 30th 2015, Feb. 23rd 2016, April 6th 2016

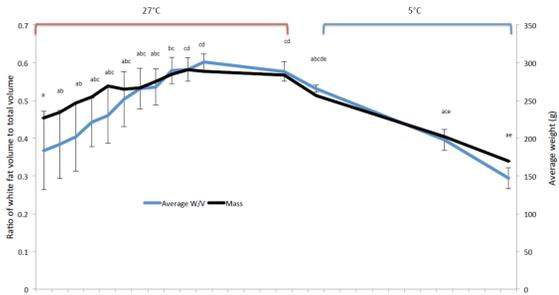


Fig 1. Changes in total WAT (blue) and mass (black)

- The visceral and subcutaneous WAT increase substantially in anticipation for hibernation, and decrease during hibernation
- WAT pattern largely mirrors changes in total body mass

Brown Adipose Tissue Volume

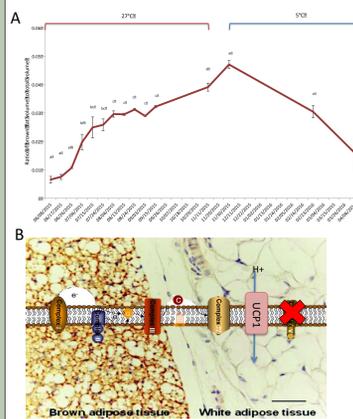


Fig 2. A) Ratio of BAT volume to whole animal volume. B) Histology of BAT.

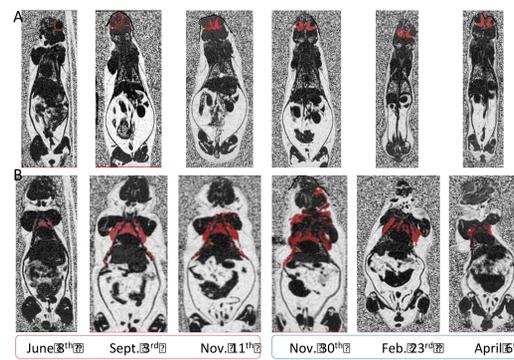


Fig 3. BAT highlighted in red in head (A) and thorax (B). Note diffuse bat distribution in thorax.

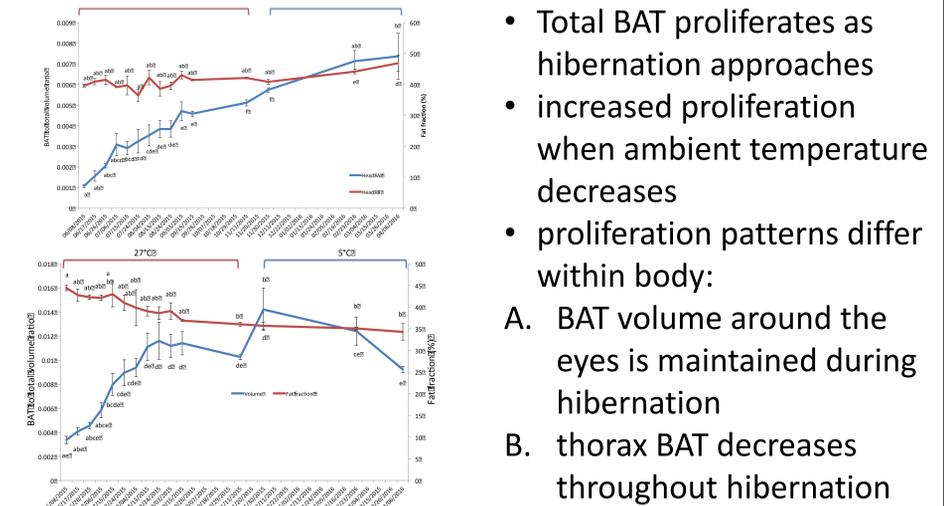


Fig 4. BAT /whole animal volume (blue) and fat fraction (red) for head (A) and thorax (B).

- Total BAT proliferates as hibernation approaches
- increased proliferation when ambient temperature decreases
- proliferation patterns differ within body:
 - BAT volume around the eyes is maintained during hibernation
 - thorax BAT decreases throughout hibernation

Fat fraction

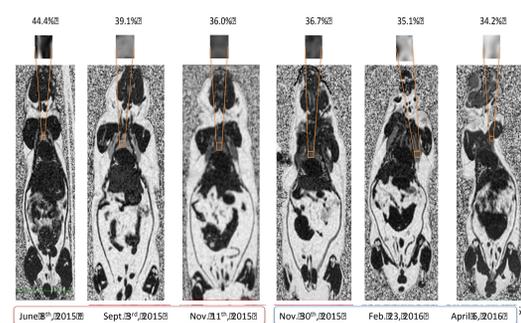


Fig 5. Thorax BAT showing fat fraction (insets).

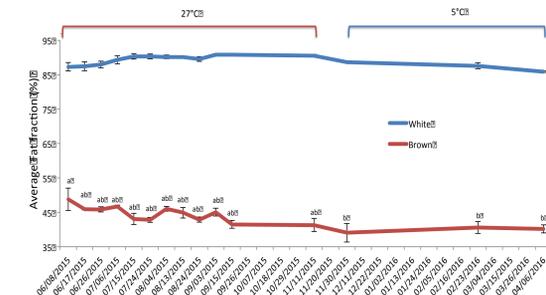


Fig 6. Fat fraction for total WAT (blue) and BAT (red).

- As hibernation approaches, total BAT fat fraction decreases
- Increase in water? Decrease in lipid?
- Changes in fat fraction differ within body:
 - Thorax BAT fat fraction decreases when temperature drops, but head BAT continues to increase

Conclusions:

- BAT proliferation occur seasonally *without* cold acclimation.
 - Cold exposure increases proliferation and decreases fat fraction, at least in thorax
 - Lipid oxidized? More mitochondria? Increased vasculature?
 - What is the role of photoperiod? Summer cold-acclimation?
- Most BAT proliferation in thorax, but also greatest decline in hibernation
 - Significant apparent BAT pad adjacent to eyes that is maintained throughout hibernation
 - Does “eye BAT” express UCP1? Western blot analysis will confirm
 - Could “eye BAT” explain reports of brain heating in hibernators?



Future Directions:
BAT dynamics in young-of-the-year.



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