

Very low-density lipoprotein triglyceride and free fatty acid clearance rates are linked to brown adipose tissue in women with overweight/obesity

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INTRODUCTION

Increased plasma triglycerides (TG) and free fatty acid (FFA) concentrations have been implicated in the pathogenesis of type 2 diabetes and coronary heart disease. Accordingly, an understanding of the mechanisms responsible for the regulation of TG and FFA metabolism has important physiological and clinical implications.

Studies conducted in rodent models have found that brown adipose tissue (BAT), which has a high oxidative capacity for fatty acids, is an important site for TG and FFA clearance from the circulation. However, the inter-relationships among BAT volume and VLDL-TG and FFA kinetics and concentrations in people are not known.

METHODS

We evaluated VLDL-TG kinetics (assessed by infusing a stable isotope glycerol tracer in conjunction with mathematical modelling) and concentrations in women with overweight/obesity who had either no/minimal BAT (LBAT, volume <20 ml, n=11) or a high amount of BAT (HBAT, volume ≥20 ml, n=14) during conditions of thermoneutrality (26-28°C). BAT was evaluated by using 2-deoxy-2-[¹⁸F] fluorogluco-¹⁸F-FDG positron emission tomography-computed tomography (PET-CT) imaging after 6 h of exposure to mild cold. Biopsy samples from supraclavicular adipose tissue (SCVAT), the primary site of brown adipocytes in people, subcutaneous abdominal ("white") adipose tissue and the vastus lateralis muscle were obtained during thermoneutrality to evaluate the expression of genes involved in lipid metabolism.

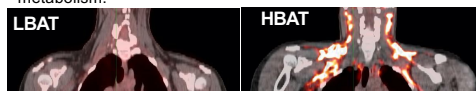


Figure 1. ¹⁸F-FDG-PET/CT imaging for BAT assessment. BAT-: participant with minimal BAT. BAT+: participant with high BAT volume.

Parameters	LBAT (n = 11)	HBAT (n = 14)
Age (years)	48.0 ± 7.7	36.0 ± 9.7*
BMI (kg/m ²)	29.4 ± 2.3	31.1 ± 2.1
Body Fat (%)	42 ± 5	45 ± 3
Fasting Serum Insulin (μU/ml)	9.8 ± 5.4	11.3 ± 5.6
Fasting Plasma Glucose (mg/dl)	88.5 ± 8.4	89.6 ± 5.7
2-h OGTT glucose (mg/dL) ^a	124 (117, 152)	122 (111, 130)
Total free fatty acid (μmol/L)	0.66 ± 0.19	0.47 ± 0.10*
Total TG (mg/dL)	97.3 (85.2, 127.4)	70.9 (51.7, 119.2)*
VLDL-TG (mg/dL)	53.3 (35.1, 61.6)	29.8 (21.0, 54.8)
BAT _{LBM} volume (ml)	3.6 (1.6, 3.6)	72.9 (44.1, 150.0)**
BAT activity (ml* SUV _{LBM} mean)	5.5 (4.7, 9.4)	256 (143, 650)**
BAT SUV _{LBM} mean	2.5 (2.3, 2.7)	3.5 (3.3, 4.1)**
BAT SUV _{LBM} max	4.0 (3.0, 4.8)	12.7 (8.9, 19.3)**

Table 1. Summary characteristics. Data are mean ± SD or median (interquartile range). OGTT: oral glucose tolerance test. SUV_{LBM}: standardized uptake value corrected for lean body mass. *p<0.01, **p<0.001.

RESULTS

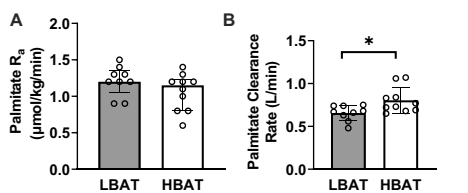


Figure 2. BAT status and free fatty acid kinetics. Data are mean and SD. *p<0.05.

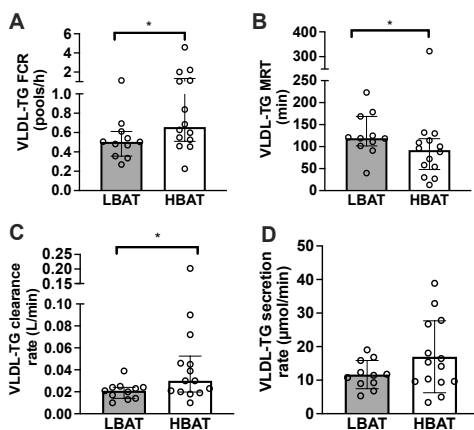


Figure 3. BAT status and VLDL-TG kinetics. FCR: fractional clearance rate, MRT: mean residence time. Data are median and interquartile range. *p<0.05.

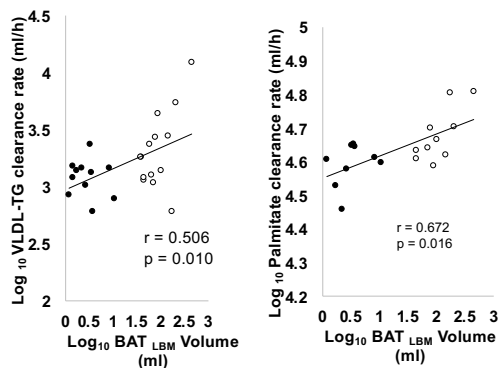


Figure 4. Relationships between VLDL-TG and FFA clearance rates with BAT volume. The correlations remained significant after adjustment for age and adiposity.

RESULTS

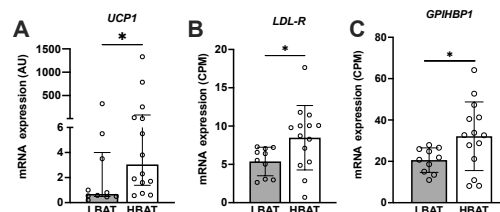


Figure 5. Expression of key genes involved in thermogenesis and lipid metabolism in the supraclavicular adipose tissue depot. Data are mean ± SD for normally distributed data or median (interquartile range) for skewed data. *p<0.05. No differences were observed in the same genes in skeletal muscle or subcutaneous abdominal adipose tissue.

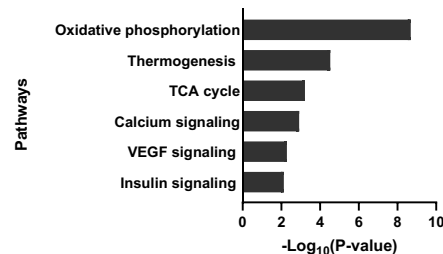


Figure 6. Differentially expressed pathways in the SCVAT of the HBAT and the LBAT group using KEGG pathway analysis. No differences in were observed pathways directly involved in lipid metabolism in skeletal muscle and subcutaneous abdominal adipose tissue.

CONCLUSION

The results from this study demonstrate that a high amount of BAT is associated with low plasma TG and FFA concentrations because of increased VLDL-TG and FFA clearance, not decreased hepatic VLDL-TG and adipose tissue FFA release into the circulation in women with overweight/obesity.

The transcriptomic analysis of SCVAT (primary location of human BAT) demonstrated differences in BAT, but not subcutaneous adipose tissue or muscle lipid uptake and oxidation between the HBAT and LBAT group.

Taken together, these findings provide further evidence on the potential significance of human BAT in the regulation of lipid metabolism in women with excessive adiposity.

Acknowledgements: This project was funded by the BJC Foundation. MC was funded by the American Heart Association.