Ethnic Differences in Fatty Acid Oxidation

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Introduction: The Triglyceride Paradox[1]

Triglyceride levels of African Americans are significantly lower than those of Caucasians. A visual representation of this difference is show in the graph on the right. This discrepancy in triglyceride level complicates the recognition and diagnosis of metabolic disease in African Americans.[1,3-6] Although lower levels of plasma triglycerides would seem to be a protective metabolic marker, metabolic and cardiovascular disease prevalence is not lower in the African American population when compared to the Caucasian population.[7] Thus, the phenomenon of lower triglycerides represents a paradox in the metabolic and cardiovascular health of African Americans.

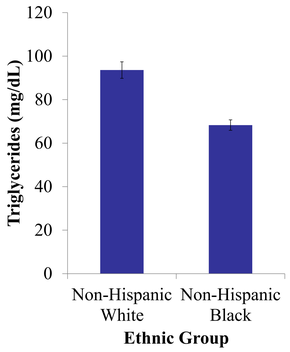
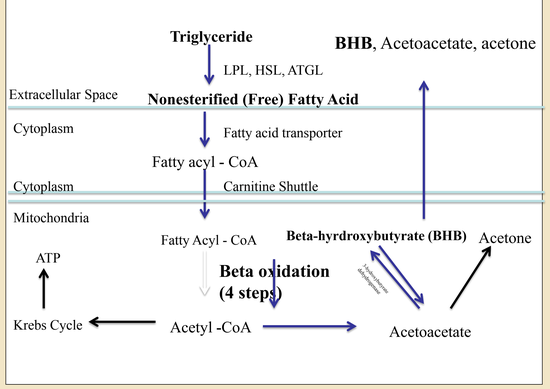


Figure 1. Triglyceride levels of NHANES volunteers, aged 12-19, from 1999-2008, n=3693.2

Many reasons for this difference in triglycerides have been explored including increased lipoprotein lipase (LPL) activity, decreased hepatic lipase (HL) activity, and increased suppression of adipocyte lipolysis.[1,8,9] Another possible explanation for this triglyceride discrepancy that has not been explored in depth is a **difference in fatty acid oxidation** between the two groups. The relevant biochemistry of fatty acid oxidation in the liver is reviewed in the figure below.

Simplified Model of Triglyceride Metabolism (Liver)



Study Hypothesis

The hypothesis of the present study is that the discrepancy in triglycerides between African Americans and Caucasians can be explained, at least in part, by more efficient beta oxidation of fatty acids in the African American population when compared to the Caucasian population.

Volunteer Screening

Volunteers were screened by clinical history and physical exam, anthropologic measurements (waist circumference, hip circumference, height, and weight), and baseline laboratory screening (fasting lipid panel, complete blood count, complete metabolic profile, thyroid stimulating hormone, and creatinine phosphokinase).

Inclusion and Exclusion Criteria

Inclusion criteria included male gender, age 18-75, and waist circumference < 90 cm

Exclusion criteria for the study include female gender and waist circumference >90cm. Volunteers were also excluded if they had history of metabolic disease or diabetes. Patients with signs of metabolic disease on labs (fasting glucose > 100mg/dL or fasting triglycerides > 150 mg/dL) were excluded.Volunteers were excluded if they had history of kidney disease (or eGFR<60), liver disease (or LFTs> 1.5*ULN), heart disease, untreated hypertension, and untreated thyroid disease (or TSH <0.5 or >4.5). Volunteers with history of alcohol or drug dependence, HIV, and hepatitis were excluded. Medications that warranted exclusion included hypolipidemic medications, hypoglycemic medications, and steroids. Volunteers with anemia (Hb<10g/dL) were excluded from the study.

Fat Tolerance Test

Fat load used: Schepp's dairy heavy whipping cream

40% w/v fat emulsion

Ratio of polyunsaturated fat to saturated fat: 0.06

0.001% w/v cholesterol and 2.8% w/v carbohydrates

Amount of cream: 200mg/kg/hr to be given every hr for 10hr period. Cream was given immediately following blood collection.

Timing of blood draws: -30min, -15min, 0min, 30min, 1hr, 2hr, 3hr, 4hr, 5hr, 6hr, 7hr, 8hr, 9hr, 10hr

Venous blood was drawn from pre-warmed hand vein to arterialize blood.

Plasma was immediately separated in a refrigerated centrifuge, aliquoted into vials on dry ice, and subsequently frozen stored at -80 ℃

Data Analysis

3-beta hydroxybuterate (BHB), non-esterified fatty acid (NEFA), plasma triglycerides (TAG) were measured for each time point during the test. Samples were analyzed within 72 hours of collection.

The data were plotted against time and area under the curve (AUC) was calculated for each plot using the trapezoid rule. The ratio of BHB to NEFA total AUC was calculated and compared between groups. One volunteer from the Caucasian group was excluded from analysis as an outlier based on fasting BHB levels (Grubb's test p<0.01). Groups were compared using 2 sample t-tests.

Baseline Characteristics

	Caucasians n=8	African Americans n=9
Age (yrs)	31 ± 16	37 ± 15
BMI	23 ± 3	24 ± 2
Waist Circumference (cm)	80 ± 7	80 ± 8
Waist to Height Ratio	0.44 ± 0.03	0.45 ± 0.04
Hip Circumference (cm)	97 ± 9	92 ± 7
Triglycerides (mg/dL)	80 ± 21	53 ± 13
LDL cholesterol (mg/dL)	104 ± 27	88 ± 37
HDL cholesterol (mg/dL)	50 ± 9	58 ± 18
Fasting glucose (mg/dL)	87 ± 8	88 ± 9

Fat Tolerance Test Results

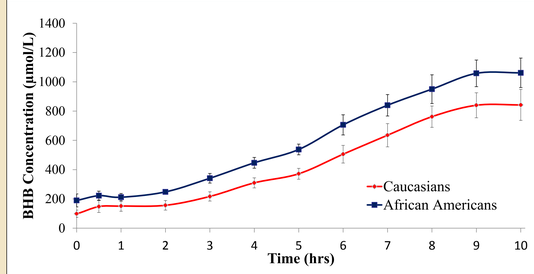


Figure 2. Concentration of 3-beta hydroxybuterate (BHB) over time during the fat tolerance test. Data are plotted as Mean ± Standard Error of the Mean.

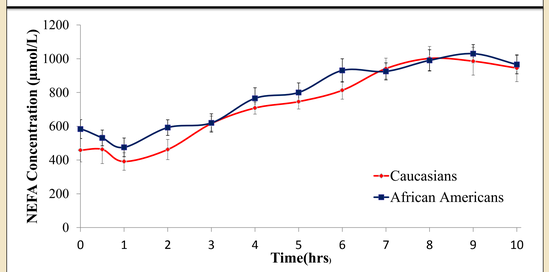


Figure 3. Concentration of non-esterified fatty acid (NEFA) over time during the fat tolerance test. Data are plotted as Mean ± Standard Error of the Mean.

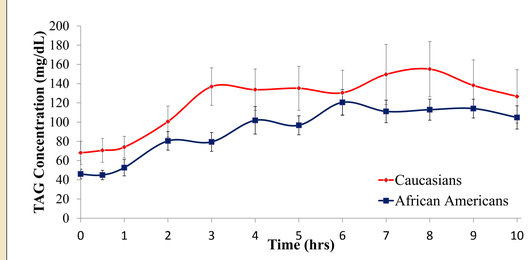


Figure 4. Concentration of plasma triglycerides (TAG) over time during the fat tolerance test. Data are plotted as Mean ± Standard Error of the Mean.

Results (continued)

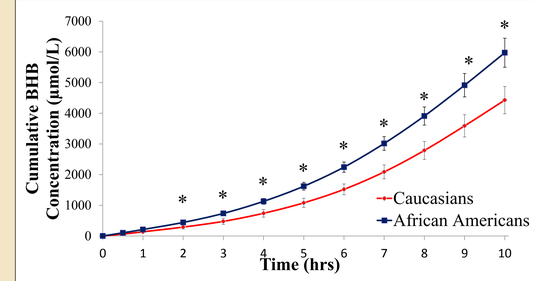


Figure 5. Cumulative plot of the area under the curve (AUC) of the concentration of 3-beta hydroxybuterate (BHB) over time. Data are plotted as Mean ± Standard Error of the Mean.

* Denotes p<0.05 at the given time point.

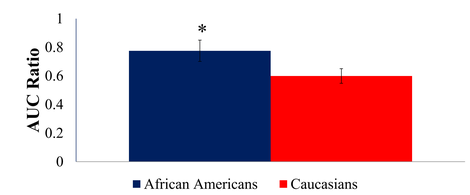


Figure 6. Ratio of the total Area under the Curve (AUC) of the concentration of 3-beta hydroxybuterate (BHB) to the total AUC of non-esterified fatty acid (NEFA). Data are plotted as Mean ± Standard Error of the Mean.

* Denotes p<0.05

Conclusion

Preliminary results suggest that healthy lean African American men may be more efficient oxidizers of fatty acids when compared to healthy lean Caucasian men. This difference could be a contributing factor to the triglyceride difference observed in African Americans and Caucasians. Recruitment for and analysis of this study is ongoing at this time.

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Acknowledgements

I would like to thank Dr. Grundy, Dr. Vega, and Dr. Szuszkiewicz-Garcia for their continued mentorship and support throughout this project.

This work was conducted with support from the Center for Translational Medicine, NIH/NCATS Grant Number TL1TR001104. The content is solely the responsibility of the authors and does not necessarily represent the official views of Center for Translational Medicine, UT Southwestern Medical Center and its affiliated academic and health care centers, the National Center for Advancing Translational Sciences, or the National Institutes of Health

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