

At Risk Alcohol Use and Impaired Glucose Tolerance Decrease Skeletal Muscle Mitochondrial Function in People Living with HIV

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Introduction

- At-risk alcohol use is nearly 2x as prevalent among people living with HIV (PLWH)
- With antiretroviral therapy (ART), PLWH have near-normal life expectancy, increasing incidence of metabolic comorbidities (e.g. insulin resistance)
- At-risk alcohol use & HIV are independently associated with skeletal muscle (SKM) dysfunction
 - Key determinate of energy homeostasis & resting metabolism
- Mitochondrial dysregulation may contribute to SKM dysfunction & insulin resistance
 - ↑ risk for glucose intolerance
 - Mitochondrial gene expression provides insight into dysregulated mitochondrial processes

Hypothesis

At-risk alcohol consumption and dysglycemia alter SKM expression of genes involved in mitochondrial biogenesis and function in PLWH

Methods

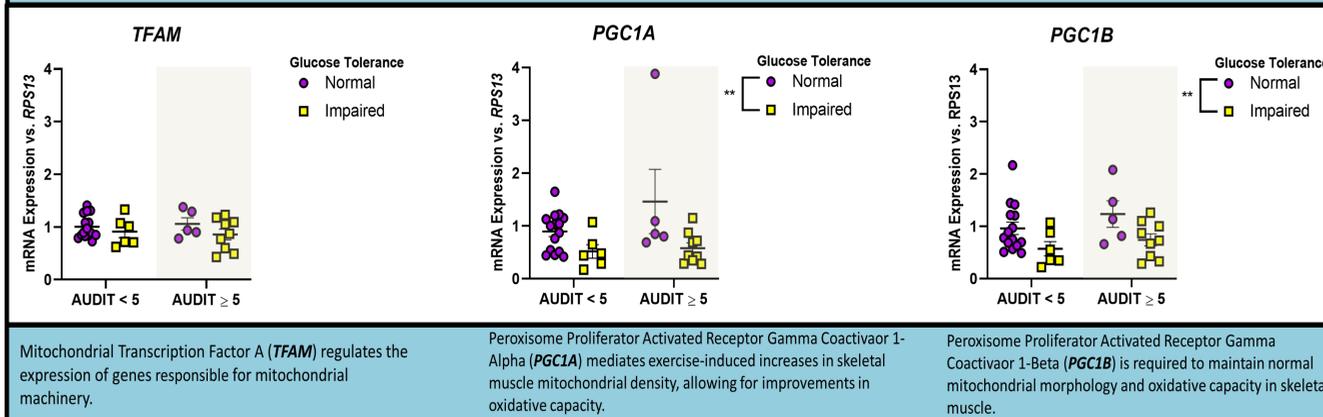
- PLWH provided informed consent to participate
- Completed AUDIT to identify at-risk alcohol use
 - AUDIT < 5
 - AUDIT ≥ 5
- OGTT to assess glucose tolerance (2h post-75 g glucose ingestion)
 - Normal = plasma glucose <140 mg/dl
 - Impaired = plasma glucose 140 to 200 mg/dl
- Muscle biopsy
- PCR for mitochondrial genes vs. RPS13

Cohort Demographics

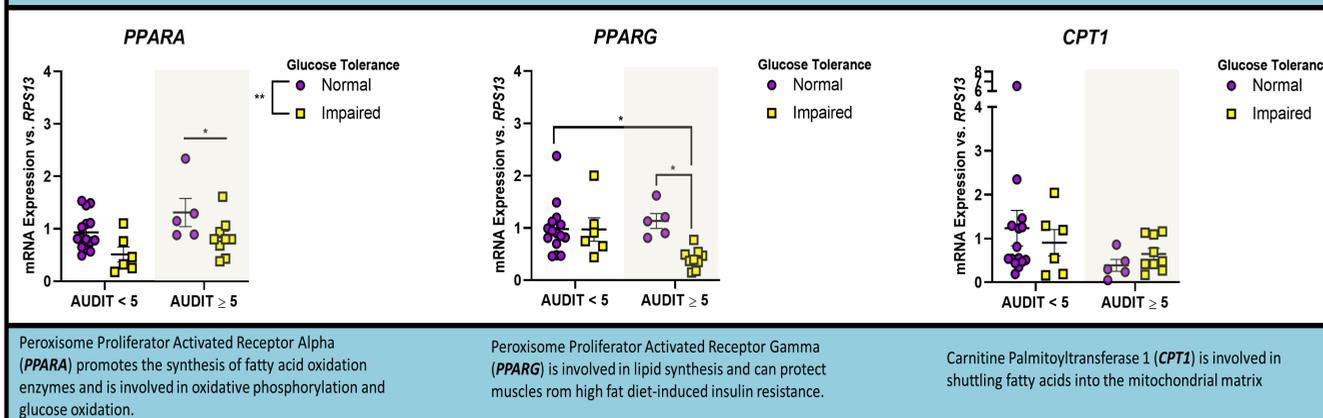
	Groups	Age (yrs)	Sex	AUDIT	BMI (kg/m ²)
AUDIT <5	Normal Glucose Tolerance	54 ± 12	M:8 F:7	1 ± 1	28.8 ± 5.6
	Impaired Glucose Tolerance	53 ± 9	M:5 F:1	2 ± 1	31.2 ± 6.3
AUDIT ≥5	Normal Glucose Tolerance	56 ± 6	M:4 F:1	12 ± 7	27.0 ± 7.3
	Impaired Glucose Tolerance	50 ± 6	M:7 F:2	11 ± 7	29.0 ± 8.4

Results

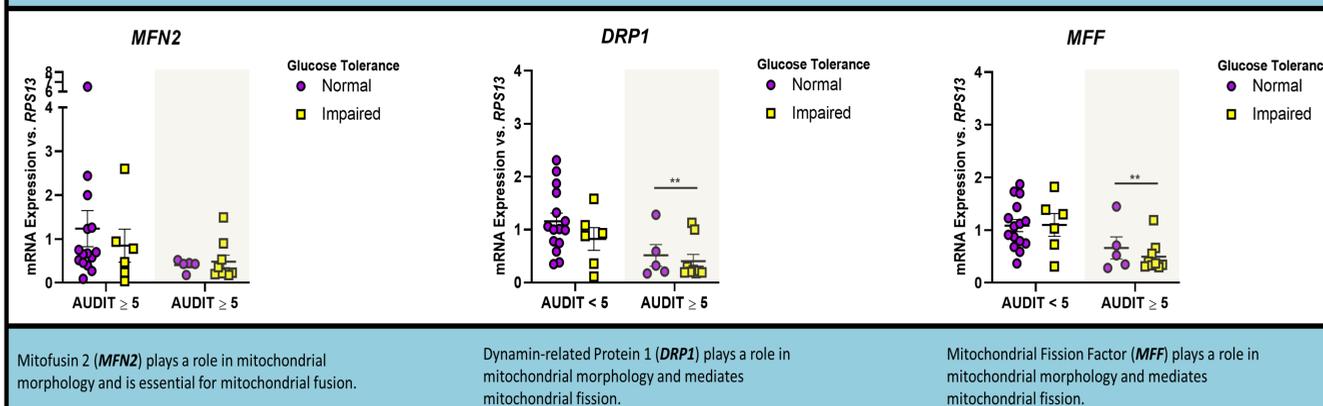
Genes Involved in Mitochondrial Biogenesis



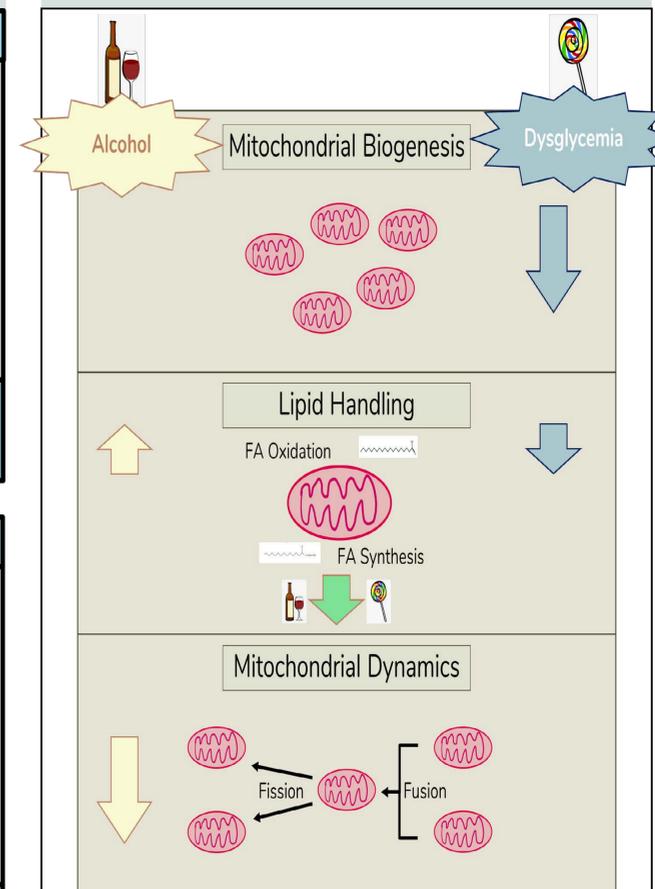
Genes Involved in Lipid Handling



Genes Involved in Mitochondrial Dynamics



Discussion



Future Directions

- Measurements of mitochondrial content
 - PCR – mtDNA in SKM
 - Mitotracker – myoblasts
- Mitochondrial function assay – Seahorse
- Mitophagy assay depending on cell availability - MitoKeima

Acknowledgments

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