Seven sessions of high-intensity interval training increased respiration of lipid and non-lipid substrates in skeletal muscle mitochondria in lean adults

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INTRODUCTION

- Skeletal muscle has a large tissue mass and high abundance of mitochondria, the major site of fuel metabolism and energy production, and contributes to whole-body metabolism.
- High-intensity interval training (HIIT) is a time-efficient training approach to improve whole-body metabolism in part through skeletal muscle mitochondria adaptations.
- Whether short-term HIIT is sufficient to induce early mitochondrial remodeling to drive changes in skeletal muscle mitochondrial function and whole-body substrate oxidation remains poorly understood.

OBJECTIVE

We investigated the impact of short-term HIIT on whole-body and skeletal muscle mitochondria substrate oxidation in healthy adult humans.

METHODS

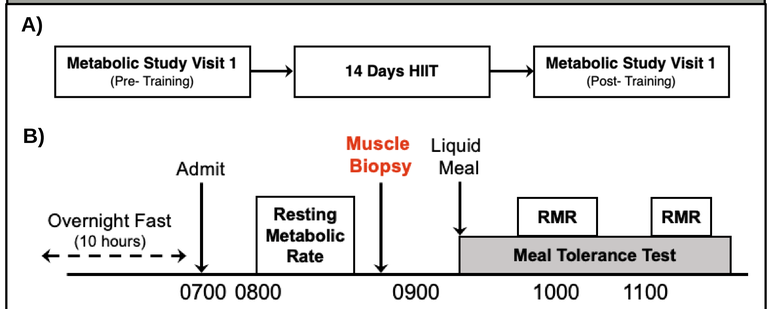

Figure 1 – Study Design: A) Overall study timeline and **B)** metabolic study visit. Participants (n=14) completed the same study day before and after short-term HIIT, a muscle biopsy was collected each day for subsequent mitochondrial respiration and western blot analysis. Resting metabolic rate (RMR)

- **Study Days:** Sedentary lean adults (n=14) (characteristics in table 1) completed two study days, one at baseline and one 24 hours after the final HIIT session. Each day consisted of resting metabolic rate (RMR) to measure whole-body energy expenditure, indirect calorimetry during a 2-hour mixed meal tolerance test to measure energy expenditure and substrate oxidation, and a muscle biopsy.
- **Exercise:** Following the first study day, participants completed seven HIIT sessions in 14 days. Each HIIT session was ten 1-minute bouts of cycling at 90% maximal heart rate interspersed with 1 minute of rest.
- **Mitochondrial respiration:** High resolution respirometry (Oroboros Instruments, Innsbruck, Austria) was performed on isolated mitochondria from the quadriceps with distinct analyses using non-lipid and lipid substrates.
- **Markers of Mitochondrial Protein, and Lipid Oxidation:** CI, CII, CIII, CIV, CV, HADH, protein abundance were determined via western blot.

RESULTS

Participant Characteristics

Sex	6M/8F
Age (years)	27 ± 7 (18-41)
Height (m)	1.7 ± 0.1 (1.5-1.9)
Weight (kg)	65.0 ± 11.8 (49.0-86.6)
BMI (kg/m^2)	22.1 ± 2.1 (18.8-24.8)
Body fat (%)	26.5 ± 7.5 (15.2-41.7)
$VO_{2\ peak}$ (L/min)	2.3 ± 0.7 (1.19-3.61)
$VO_{2\ peak}$ (ml/kg/min)	35.9 ± 8.5 (17.6-50.2)
REE (kcal/min)	1524 ± 247 (1164-2005)
ΔPO (%)	*30.0 ± 0.20 (0.0-67.0)

Table 1: Body mass index (BMI), Resting energy expenditure (REE), percent change in power output from first to last HIIT session (ΔPO). Mean ± SD (range). *P<0.05 t-test (1st to 7th HIIT session)

HIIT tended to increase change in whole body substrate oxidation in response to mixed-meal consumption

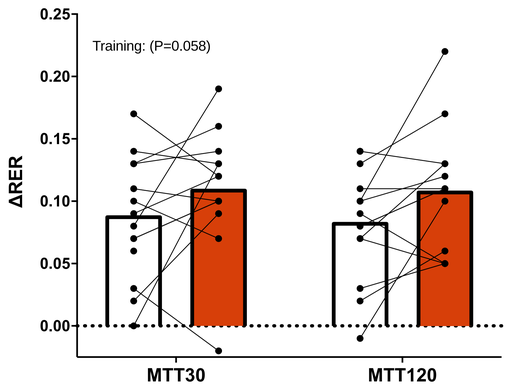

Figure 3: Change in respiratory exchange ratio from baseline during a mixed-meal tolerance test. Data are mean and individual values analyzed by 2-way ANOVA, P values are main effects. Abbreviations: ΔRER – change in respiratory exchange ratio from rest; MTT30, MTT 120– 30 and 120 minutes after consumption of mixed meal, respectively.

HIIT increased skeletal muscle mitochondrial respiration of lipid and non-lipid substrates

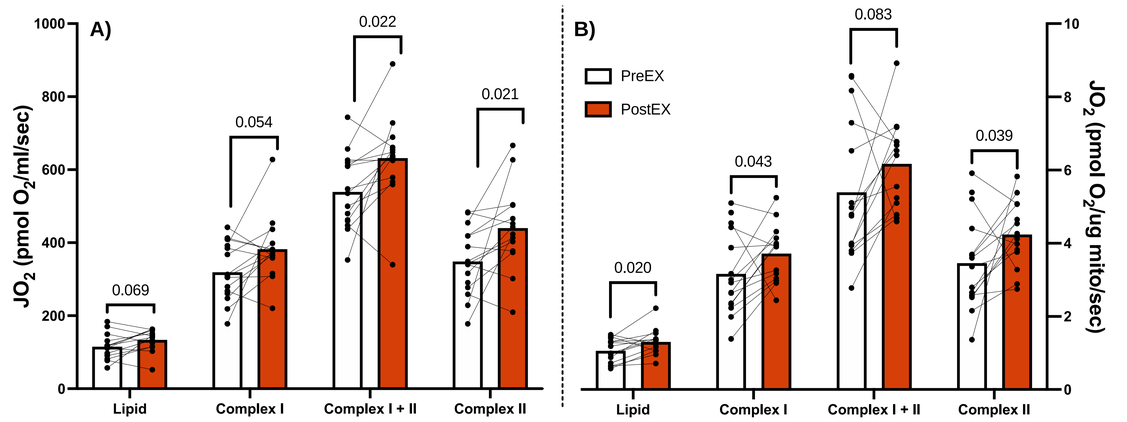

Figure 2: Mitochondrial respiration in response to lipid and non-lipid substrates. A) Absolute (pmol/ml/sec) and **B)** normalized (pmol/µg protein/sec) mitochondrial respiration. Data are mean and individual values and analyzed via paired T-Tests, α = 0.05. Substrates and inhibitors addition include octanoylcarnitine for lipid supported respiration (Lipid), malate and glutamate for Complex I respiration, succinate for Complex I + II respiration, and rotenone to inhibit complex I and determine Complex II respiration.

HIIT did not change protein content of markers related to mitochondria, or lipid oxidation

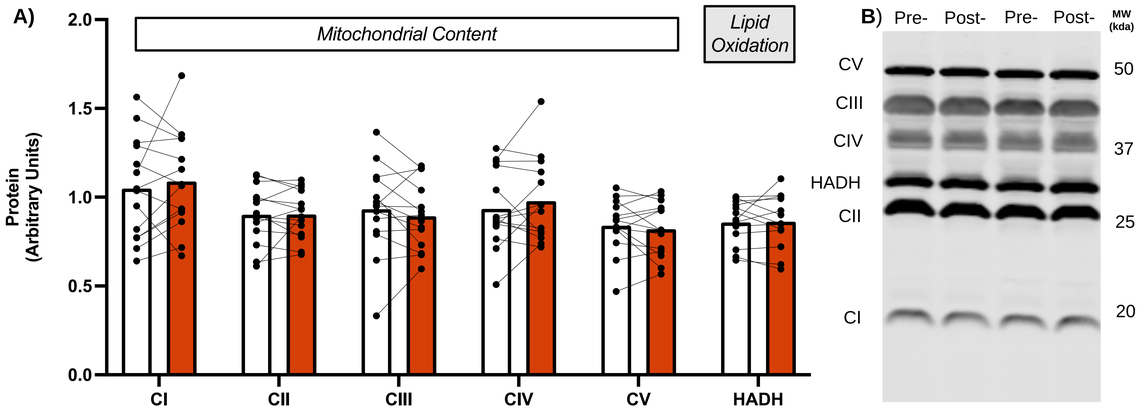

Figure 4: Protein content of mitochondrial, and lipid oxidation markers before and after HIIT with representative blot images. **A)** Protein content and **B)** representative blot image. Data are mean and individual values, analyzed via paired T-Tests, α = 0.05. Mitochondrial markers included complex I (CI), complex II (CII), complex III (CIII), complex IV (CIV), complex V (CV); lipid markers included Hydroxyacyl-Coenzyme A dehydrogenase (HADH); molecular weight (MW)

SUMMARY & CONCLUSION

- Seven sessions of high intensity interval training over 14 days increased whole body metabolic flexibility and skeletal muscle mitochondrial respiration in lean, sedentary, healthy adults.
- Skeletal muscle mitochondrial respiration increased for lipid and non-lipid substrates, without changes to specific subunits representative of mitochondrial/electron transport complexes indicating potential change to function without change in abundance.
- Next steps include further investigation into the mechanisms facilitating increases to whole-body and skeletal muscle specific metabolism. We will investigate activation of protein degradation (via autophagy) in the early remodeling response of mitochondria to exercise.

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