

Article Title

Exercise training results in depot-specific adaptations to adipose tissue mitochondrial function.

Authors

Mendham, Amy E., Larsen, Steen., George, Cindy., Adams, Kevin., Hauksson, Jon., Olsson, Tommy., Fortuin-
de Smidt, Melony C., Nono Nankam, Pamela, Hakim, Olah, Goff, Louise M, Pheiffer, Carmen, Goedecke, Julia
H

Supplementary table 1: Energy expenditure and consumption at baseline, weeks 4, 8 and 12 of the intervention.

Variable	EXERCISE				CONTROL				Time P Value	Group P Value	Interaction P Value
	Baseline	Week 4	Week 8	Week 12	Baseline	Week 4	Week 8	Week 12			
Energy expenditure (kJ/day) ¹	2426 (2266,3025)	2160 (1734,2940)	2640 ± 959	2736 ± 792	2501 (2346,3149)	2831 (2400,3544)	2916 ± 964	2837 ± 966	0.722	0.335	0.285
Metabolic Equivalents (h/day)	1.15 (1.11,1.18)	1.10 (1.08,1.20)	1.15 ± 0.08	1.15 ± 0.05	1.13 (1.09,1.17)	1.16 (1.09,1.21)	1.15 ± 0.05	1.14 ± 0.06	0.544	0.975	0.869
Energy Intake (kJ/day)	8369 (6984,11079)	8132 ± 2042	8765 ± 2178	8615 ± 1668	8138 (6493,9434)	7883 ± 1338	7880 ± 1857	8661 ± 1354	0.267	0.434	0.632
Carbohydrates (%EI)	55.1 ± 5.5	53.9 ± 5.9	54.2 ± 5.3	52.7 ± 8.3	54 ± 5.7	56.9 ± 6.0	56.0 ± 7.6	57.8 ± 7.2	0.913	0.202	0.322
Fats (%EI)	30.4 ± 6.1	31.0 ± 6.0	31.3 ± 5.5	32.2 ± 5.9	31.0 ± 5.6	29.2 ± 5.1	30.0 ± 7.3	27.9 ± 6.4	0.970	0.485	0.235
Protein (%EI)	13.2 ± 2.5	13.9 ± 2.9	13.4 ± 2.0	13.7 ± 3.0	14.3 ± 1.9	13.2 ± 2.3	13.8 ± 2.8	13.6 ± 2.1	0.995	0.845	0.575

Normally distributed data reported as Mean ± Standard Deviation and skewed data reported as Median (Interquartile Range; IQR). Repeated-measures ANOVA identified main effects of time (pre and post) and group (exercise and control), and interactions (group x time) effect for exercise (n=20) and control (n=15) groups. Physical activity on non-exercise training days in the exercise group¹. EI, Energy Intake.

Supplementary Table 2: Adipose tissue gene expression that represent mitochondrial content, insulin signalling, lipolysis, lipogenesis and inflammation pre and post 12-week intervention.

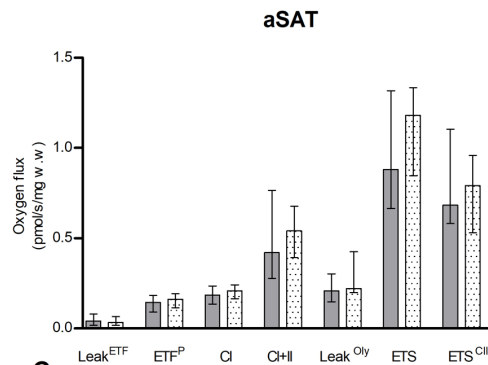
Variable	BASELINE	EXERCISE		CONTROL		Time P Value	Group P Value	Interaction P Value
		Pre	Post	Pre	Post			
Abdominal Subcutaneous Adipose Tissue								
Mitochondrial content								
Mitochondrial DNA (AU)	2.25 (1.92,3.18)	2.5 (1.9,3.2)	2.1 (1.5,2.7)	2.0 (1.6,3.0)	1.9 (1.8,2.5)	0.211	0.544	0.247
Insulin Signalling								
Glut4 mRNA (AU)	1.39 (1.00,2.14)	1.39 (0.61,2.82)	1.73 (1.24,2.25)	1.18 (1.01,1.64)	1.90 (1.15,3.17)	0.002	0.677	0.990
IRS1 mRNA (AU)	1.32 (0.95,2.10)	1.40 (0.91, 2.10)	1.28 (0.90,1.98)	1.11 (0.85,1.78)	1.30 (0.82,1.76)	0.918	0.365	0.113
PI3K mRNA (AU)	1.43 ± 0.51	1.28 (1.03,1.66)	1.20 (1.00,1.87)	1.35 (1.05,1.66)	1.20 (0.72,1.72)	0.918	0.365	0.113
Adiponectin mRNA (AU)	0.78 ± 0.33	0.76 (0.43,0.93)	0.62 (0.40, 0.88)	0.78 (0.52,0.98)	0.53 (0.48,0.69)	0.016	0.650	0.611
PPAR-γ mRNA (AU)	1.06 ± 0.46	1.14 (0.78,1.39)	0.85 (0.55,1.06)	0.90 (0.62,1.37)	0.78 (0.63,1.30)	0.073	0.945	0.297
Lipolysis								
ATGL mRNA (AU)	1.22 ± 0.53	0.98 (0.76,1.72)	0.95 (0.61,1.23)	1.45 (0.97,1.78)	1.08 (0.78,1.38)	0.069	0.486	0.239
Lipogenesis								
LPL mRNA (AU)	1.01 ± 0.40	0.94 (0.79,1.21)	0.74 (0.55,1.10)	1.07 (0.75,1.26)	0.75 (0.61,0.89)	0.035	0.592	0.654
DGAT2 mRNA (AU)	0.93 (0.64,1.77)	0.73 (0.24,2.17)	1.59 (0.94,3.00)	0.93 (0.71,1.89)	1.57 (0.83,2.39)	0.076	0.997	0.632
Perilipin 1 mRNA (AU)	2.00 (1.16,3.10)	1.69 (1.01,2.47)	1.56 (1.22,2.57)	2.22 (1.59,3.08)	1.57 (1.14,2.38)	0.259	0.527	0.373
Inflammation								
NF-κB1 mRNA (AU)	1.36 (1.08,2.1)	1.23 (1.01,2.15)	1.51 (1.01,2.04)	1.32 (0.96,1.63)	1.04 (0.90,1.59)	0.957	0.537	0.196
TNF-α mRNA (AU)	0.90 (0.55,1.32)	0.93 (0.54,1.31)	1.33 (0.65,1.72)	0.72 (0.54,1.03)	0.95 (0.75,1.43)	0.004	0.722	0.992
Catalase mRNA (AU)	1.77 ± 0.58	1.67 ± 0.59	1.61 ± 0.56	1.63 ± 0.54	1.66 ± 0.36	0.226	0.335	0.626
Gluteal Subcutaneous Adipose Tissue								
Mitochondrial content								
Mitochondrial DNA (AU)	2.19 ± 0.45	2.4 (2.2,2.6)	2.2 (1.6,2.4)	2.2 (1.9,2.9)	2.0 (1.9,2.5)	0.031	0.749	0.719
Insulin Signalling								
Glut4 mRNA (AU)	1.43 (0.99,1.98)	1.41 (0.89,2.07)	1.69 (1.19,2.27)	1.38 (1.17,1.71)	1.62 (0.79,2.85)	0.265	0.966	0.521
IRS1 mRNA (AU)	1.73 (1.36,2.19)	1.24 (0.91,1.53)	1.28 (1.05,1.56)	1.08(0.92,1.62)	1.12 (0.94,1.85)	0.705	0.569	0.626
PI3K mRNA (AU)	1.38 (1.11,1.79)	1.32 (1.09,1.53)	1.42 (1.19,1.86)	1.49 (1.11,1.81)	1.15 (1.00,1.92)	0.892	0.215	0.735
Adiponectin mRNA (AU)	0.69 (0.52,0.96)	0.68 (0.56,0.77)	0.64 (0.50,0.83)	0.84(0.50,1.09)	0.52 (0.47,0.66)	0.029	0.628	0.161
PPAR-γ mRNA (AU)	1.12 ± 0.43	1.03 (0.84,1.39)	0.98 (0.84,1.22)	1.20 (0.81,1.35)	0.82 (0.64, 1.46)	0.276	0.720	0.407
Lipolysis								
ATGL mRNA (AU)	1.35 (1.09,2.19)^	1.39 (1.05,1.70)	1.17 (0.86,1.48)	1.53 (1.00,2.55)	1.19 (0.91,1.49)	0.003	0.630	0.393
Lipogenesis								
LPL mRNA (AU)	1.02 (0.73,1.39)	1.03 (0.81,1.33)	0.81 (0.67,1.15)	1.34 (0.82, 1.51)	1.06 (1.38,0.70)	0.071	0.455	0.654
DGAT2 mRNA (AU)	1.35 (0.83,1.79)	1.29 (0.72,1.92)	1.23 (1.02,1.94)	1.53 (0.99,2.39)	1.23 (0.59,2.29)	0.531	0.739	0.802
Perilipin 1 mRNA (AU)	1.97 ± 0.65	1.76 (1.44,2.39)	1.17 (0.86,1.48)	1.97 (1.30,2.41)	1.59 (1.22,2.48)	0.153	0.948	0.642
Inflammation								
NF-κB1 mRNA (AU)	1.35 (1.08,1.62)	1.41 (1.22,1.60)	1.53 (1.27,1.97)	1.33 (1.00,1.67)	1.04 (0.80,1.30)	0.417	0.040	0.087

TNF- α mRNA (AU)	1.07 (0.73,1.16)	1.07 (0.85, 1.31)	1.31 (0.93, 1.94)	0.80 (0.56,1.15)	0.80 (0.46,1.38)	0.870	0.026	0.301
Catalase mRNA (AU)	1.78 $\pm$ 0.53	1.72 $\pm$ 0.54	1.56 $\pm$ 0.47	1.72 $\pm$ 0.57	1.70 $\pm$ 0.57	0.324	0.739	0.426

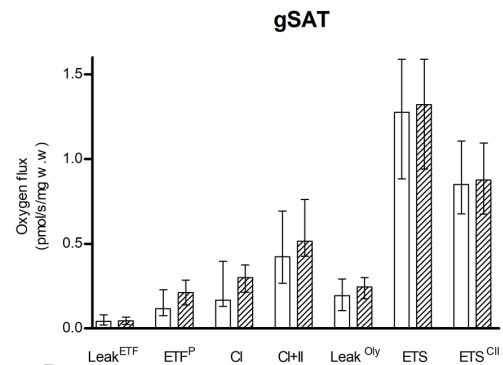
Normally distributed data reported as Mean $\pm$ Standard Deviation and skewed data reported as Median (Interquartile Range; IQR). Paired t-tests identified differences at baseline between depots (n=37). Repeated-measures ANOVA identified main effects of time (pre and post) and group (exercise and control), and interaction (group x time) effects reported for exercise (n=18 in abdominal and n=19 in gluteal depots) and control (n=14, both depots) groups. Difference between depots at baseline $^{\wedge}$ <0.05. Glut4, Glucose transporter 4; IRS1, Insulin receptor substrate 1; PI3K, Phosphoinositide 3-Kinase; ATGL, Adipose triglyceride lipase; Lipoprotein lipase; DGAT1, Diacylglycerol O-acyltransferase; PPAR, Peroxisome proliferator-activated receptors.

Supplementary Figure 1.

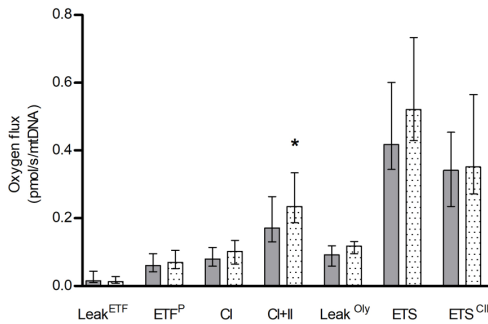
A



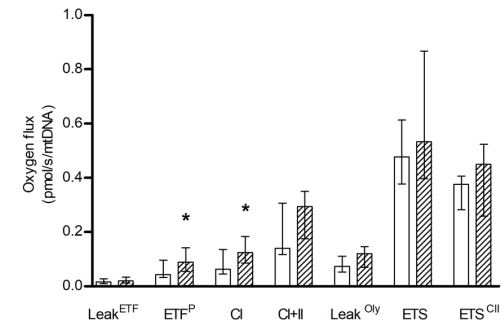
B



C



D

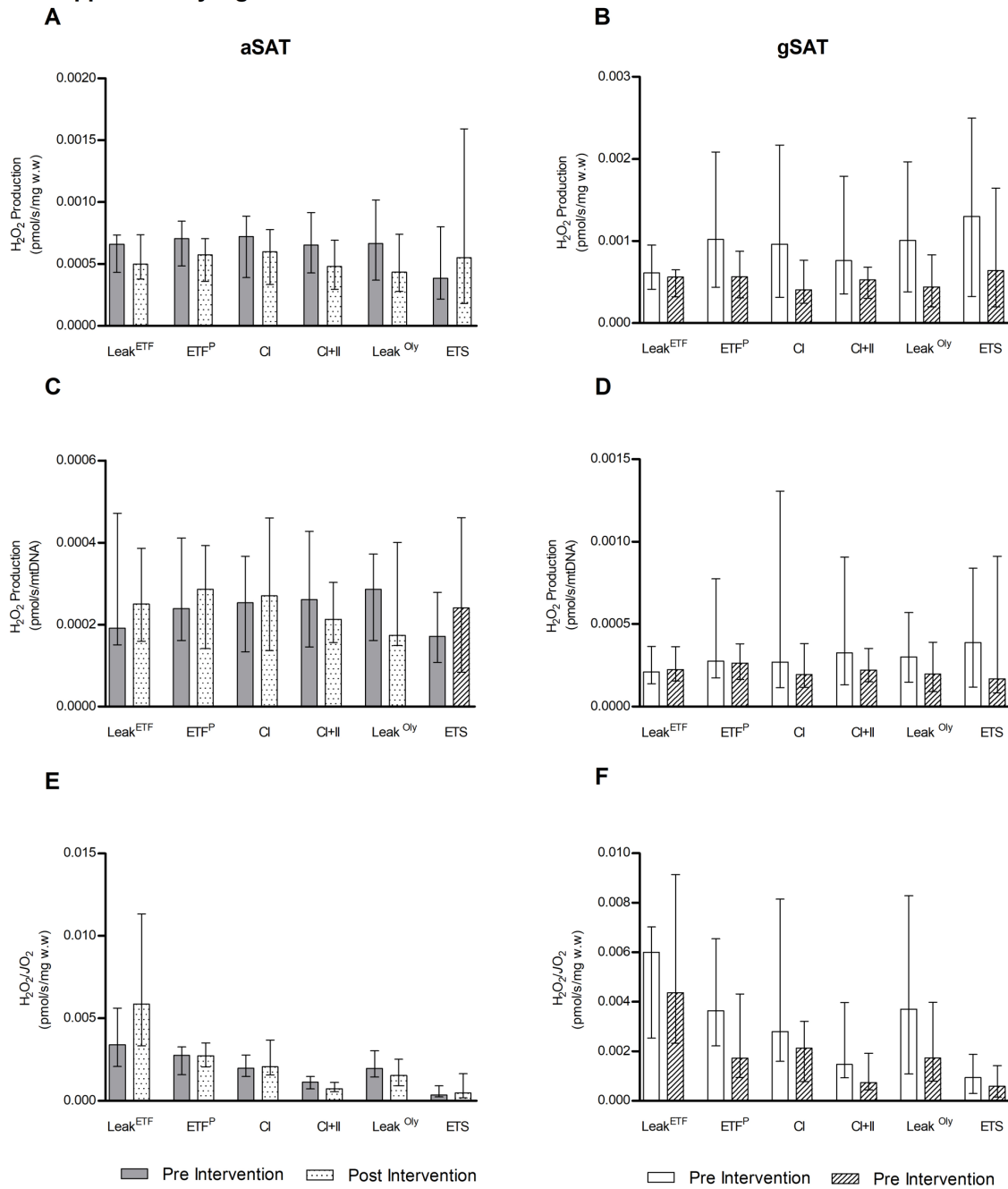


■ Pre Intervention ▨ Post Intervention

□ Pre Intervention ▨ Post Intervention

Supplementary Figure 1: Change in mitochondrial respiration in the control group over the 12-week intervention. A, C and E represent change in abdominal subcutaneous adipose tissue (aSAT). B, D and F represent change in gluteal SAT (gSAT). Mixed-model analyses identified main effects of time (pre and post) and group (exercise and control) and interaction (group x time) effects in exercise (n=19, both depots) and control (n=14 in abdominal and n=13 in gluteal depots) groups. All data reported as median (interquartile range). Significant difference between pre and post intervention in control group *p<0.05. Leak^{ETF}, leak respiration through electron-transferring flavoprotein; ETF^P, Lipid oxidative phosphorylation capacity; CI, Complex 1 linked respiration; CI+II, Complex 1 and 2 linked respiration (oxidative phosphorylation capacity); Leak^{Oly}, Oligomycin (ATP synthase inhibitor) linked leak respiration; ETS, Electron transfer system capacity; ETS^{II}, Complex 2 linked electron transfer system capacity.

Supplementary Figure 2.



Supplementary Figure 2: Change in mitochondrial H_2O_2 production in the control group over the 12-week intervention. A, C and E represent change in abdominal subcutaneous adipose tissue (aSAT). B, D and F represent change in gluteal SAT (gSAT). Mixed-model analyses identified main effects of time (pre and post) and group (exercise and control) and interaction (group x time) effects in exercise ($n=19$, both depots) and control ($n=14$ in abdominal and $n=13$ in gluteal depots) groups. All data reported as median (interquartile range). No significant differences shown between over the intervention in the control group. Leak^{ETF} , leak respiration through electron-transferring flavoprotein; ETF^{P} , Lipid oxidative phosphorylation capacity; CI, Complex 1 linked respiration; CI+II, Complex 1 and 2 linked respiration (oxidative phosphorylation capacity); Leak^{Oly} , Oligomycin (ATP synthase inhibitor) linked leak respiration; ETS, Electron transfer system capacity.