

P6203

Intramyocellular lipid saturation as a new metabolic biomarker

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Background: Endurance trained athletic healthy volunteers (Athl-HV) and type 2 diabetes patients (T2D) have higher levels of lipids in their skeletal myocytes compared to healthy controls. Despite apparently similar metabolic storage, they are at opposite ends of insulin sensitivity and cardio-metabolic risk.

Purpose: We investigated if the degree of saturation of the IntraMyoCellular Lipids (IMCL) will differentiate Athl-HV from T2D; and explored if an exercise intervention will induce changes in the IMCL saturation.

Methods: Male, age matched Athl-HV and T2D were enrolled (n=25/group). Athl-HV had ≥5 years endurance training, T2D were sedentary. Subjects were studied at baseline and after an exercise intervention (4 week deconditioning in Athl-HV and supervised bike training at ≥65% of peakVO₂, 5 hours/week x 8 weeks in T2D). All subjects underwent cardio-pulmonary exercise testing (CPET), blood sampling for insulin sensitivity (QUICKI*) and single voxel 1H-magnetic resonance spectroscopy (1H-MRS) of the right vastus lateralis. 1H-MRS was acquired on 3T Philips Achieva with a 16-channel coil, point-resolved spectroscopy, variable pulse power and optimized relaxation delay water suppression and analysed in

LCModel. We derived fractional lipid mass (fLM) and fractions of saturated (fSL) and unsaturated (fUL) lipids. Data were analysed by t tests, shown as mean±SEM, statistical significance p<0.05.

Results: CPET and insulin sensitivity are presented in Table 1. T2D had higher fLM in the skeletal muscle compared to Athl-HV, at baseline (p=0.003) and after the exercise intervention (p=0.009), Figure 1A. At baseline, T2D had a different phenotype with a lower fSL and higher fUL compared to Athl-HV (82±3 vs 88±1% and 18±3 vs 12±1%, p=0.02 for both). Whilst deconditioning did not attract any significant changes in either fSL or fUL in Athl-HV (88±1 to 86±1% and 12±1 to 14±1, p=0.2), in contrast, with exercise training T2D significantly increased fSL (82±3 to 88±1%) and decreased their fUL (18±3 to 12±1%) (both p=0.01). Figure 1B and 1C.

Conclusion: We demonstrate for the first time, in vivo, significant differences in the IMCL amount and saturation between Athl-HV and T2D. IMCL saturation was changed by exercise training in T2D to mirror the phenotype seen in Athl-HV uncovering a new, independent biomarker of improved cardio-metabolic health.

CPET and insulin sensitivity results

	Athl-HV Baseline	Athl-HV Deconditioning	p value	T2D Baseline	T2D After Training	p value
VO ₂ peak, (mL/kg/min)	45.0±0.9†	41.7±0.9‡	<0.0001	23.6±0.6†	30.3±0.6‡	<0.0001
QUICKI*	0.346±0.002†	0.343±0.003‡	0.2	0.308±0.004†	0.317±0.004‡	0.02

*QUICKI: Quantitative Insulin Sensitivity Check Index; †Athl-HV vs T2D at baseline p≤0.001, ‡Athl-HV vs T2D after exercise intervention p≤0.001.

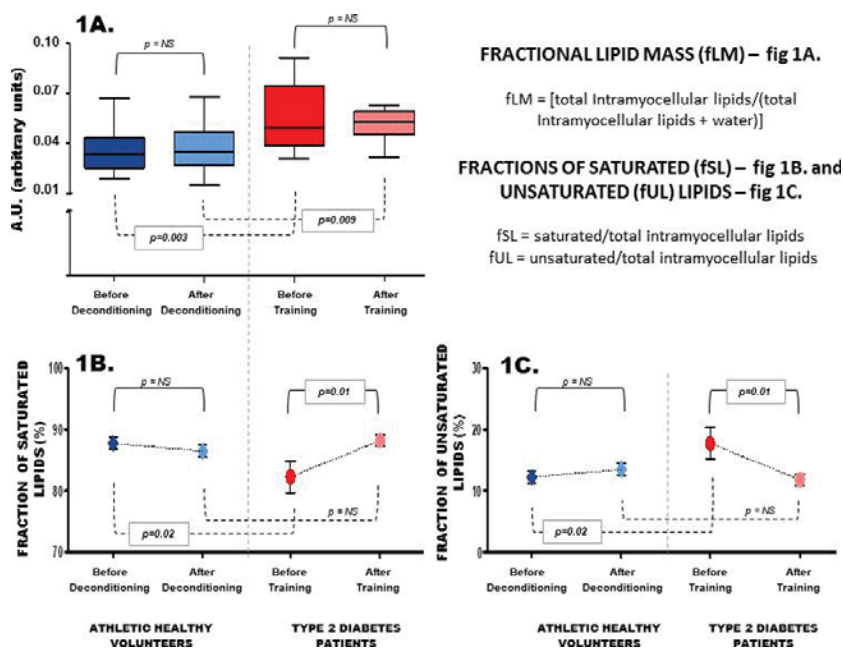


Figure 1