Resting acetylcarnitine concentration in skeletal muscle, as measured with long TE 1H-MRS, is associated with insulin sensitivity

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Introduction

Previously we showed that the use of long echo times (TE) in ^{1}H-MRS gives the opportunity to measure acetylcarnitine concentrations at rest on a 3T human MR scanner, which is available at most clinical research sites nowadays (1). This is highly interesting in the light of recent research, where whole body carnitine diminution is linked to insulin resistance and metabolic inflexibility (2). Here, we investigated skeletal muscle acetylcarnitine content in four groups, known to differ in insulin sensitivity and metabolic health.

Methods

The groups investigated comprised of type 2 diabetic patients (T2DM, N = 9), obese sedentary (OB, N = 10), lean sedentary (UT, N = 9) and endurance trained (T, N = 12) subjects. All participants were asked to remain fasted for 5 hours prior to the measurement.^{1}H-MRS was performed using a 3.0 T whole body MRI-scanner (Achieva 3T-X, Philips Healthcare, Best, The Netherlands). The subjects were positioned supine in the magnet bore, with the left leg parallel to the main magnetic field and with the foot constrained by two sandbags. A two-element flexible surface coil was placed over the vastus lateralis muscle. A PRESS (3) sequence was used for volume selection and outer volume suppression was applied to eliminate residual signals of subcutaneous adipose tissue. The voxel was placed in the vastus lateralis muscle and spectra were acquired with the following acquisition parameters: TR = 6000 ms, TE = 350 ms, spectral bandwidth = 2 kHz, number of acquired data points = 2048, number of averages (NSA) = 20, phase cycling steps = 4. Shimming was performed with standard pencil beam shimming. Voxel dimensions were 40 mm x 20 mm x 60 mm, resulting in a large volume of 48 mL. The acetylcarnitine concentration was calculated, using the total creatine (t-Cr) resonance as internal reference. Both metabolites were T_2 corrected. A hyperinsulinemic-euglycemic clamp was performed to measure insulin sensitivity (given as glucose infusion rate (GIR)). Additionally, ^{31}P-MRS was used to measure phosphocreatine (PCr) recovery rate, as a measure of *in vivo* mitochondrial function. A one-way ANOVA test, with post-hoc Bonferroni correction, was used for statistical analysis.

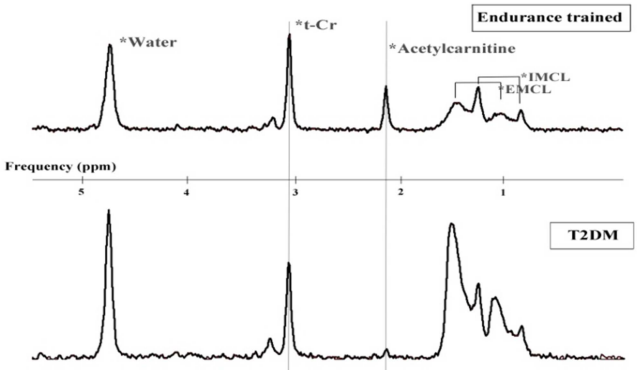

Figure 1: Two representative long TE ^{1}H-MRS spectra collected from the vastus lateralis muscle.

Results

Two representative spectra, acquired from an endurance trained athlete and a T2DM patient, respectively, are shown in figure 1. An overall difference was found across the groups for acetylcarnitine , insulin sensitivity and PCr recovery rate ($P < 0.01$ for all variables), with insulin sensitivity and mitochondrial function decreasing from trained athletes to the diabetic group and acetylcarnitine ratio showing a reciprocal distribution (table 1). The mean acetylcarnitine concentration is plotted against the mean GIR value for the four groups in figure 2. The correlation between acetylcarnitine and insulin sensitivity is highly significant ($R = 0.99$, $P = 0.01$).

	Acetylcarnitine concentration [mmol/kgww]	Insulin sensitivity (GIR) [µmol/min/kg]	PCr recovery rate [s]
T2DM	0.38 ± 0.17 (N = 9)	19.96 ± 3.65 (N = 5)	37.42 ± 3.02 (N = 8)
Obese sedentary	0.65 ± 0.16 (N = 10)	27.77 ± 5.03 (N = 10)	29.48 ± 1.69* (N = 9)
Lean sedentary	1.16 ± 0.20 (N = 9)	64.44 ± 5.78* (N = 7)	27.87 ± 0.65* (N = 9)
Endurance trained	1.42 ± 0.27* (N = 12)	86.20 ± 9.01* (N = 5)	20.72 ± 0.99* (N = 12)

Table 1: Acetylcarnitine, insulin sensitivity and PCr recovery rate for the four groups. Values are shown as mean ± SE. The asterix indicates significant differences when compared to the T2DM groups ($P < 0.05$).

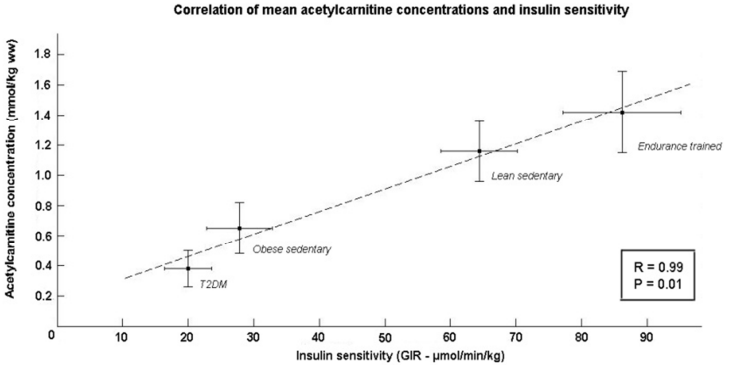

Figure 2: Mean acetylcarnitine concentration plotted versus mean insulin sensitivity in the four groups. Data are depicted as mean ± SE. Acetylcarnitine concentrations are increasing with increasing insulin sensitivity.

Discussion

Our results show differences in acetylcarnitine content across groups characterized by varying insulin sensitivity and metabolic health. The results may indicate that T2DM subjects have a lower ability to form acetylcarnitine, possibly underlying a decreased insulin sensitivity and metabolic flexibility.

References

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