Effects of a 3-month training program on muscular lipid metabolism and physical health in sedentary non-insulin-dependant diabetes mellitus patients

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Introduction: Intramyocellular lipids (IMCL) represent a major energy source of skeletal muscle. Numerous studies have shown a correlation between IMCL levels and insulin resistance. However this relationship is ambiguous, as trained athletes have been shown to be markedly insulin sensitive despite elevated IMCL levels. It is hypothesized that in trained athletes high IMCL levels are an adaptation to endurance training, whereas in obese and/or type 2 diabetes patients elevated IMCL levels are secondary to an imbalance between plasma free fatty acid (FFA) availability, storage and oxidation. Whereas there is a clear consensus that weight loss improves insulin sensitivity, the effect of increased physical activity on insulin sensitivity is less clear. Therefore, we investigated the effect of a structured training program on insulin sensitivity and skeletal muscle lipid metabolism in non-insulin-dependent diabetes mellitus type 2 (NIDDM) patients.

Methods: 9 sedentary male NIDDM patients (age: 55±7 years; BMI: 29.3±4.2 kg/m^2) with good metabolic control (HbA1c: 6.0 – 8.3%) and max. 2 oral antidiabetic drugs were investigated before and after a 3-month training program (TP). The TP consisted of three 1-hour training sessions per week (nordic-walking, aqua-fit, and gymnastics). A control group of equally sedentary age- and BMI-matched healthy volunteers was investigated once only. All participants were subject to determination of: VO_{2max} by spiroergometry, body composition by bioimpedance analysis (BIA) and sampling of fasting blood. Peripheral insulin sensitivity was determined by a euglycemic hyperinsulinemic clamp and the glucose infusion rate during the last 30 minutes of the 2 hours lasting clamp is taken as the measure for insulin sensitivity. IMCL levels were determined after a three day run-in period with high fat diet and reduced physical activity ($IMCL_{repleted}$). Short term depletion of IMCL was achieved with 3 hours exercise session (walking at constant heart rate corresponding to 50% VO_{2max} on a treadmill with 5% incline) that was split into 6 bouts of 30 minutes with interrupts of 12±1 minutes for MRS measurements. $IMCL_{repleted}$ and IMCL levels after the exercise session ($IMCL_{depleted}$) were non-invasively measured in tibialis anterior muscle with single voxel (11×12×18mm^3) ^{1}H-MR-spectroscopy (PRESS sequence, TR=3s, TE=20ms, 128 acquisitions).

Table 1: Clinical Data

		Diabetes patients pre	Diabetes patients post	p-value pre vs. post	Controls
Weight	[kg]	96.2 ± 15.4	94.9 ± 15.0	0.05	89.4 ± 12.7
BMI	[kg/m2]	29.9 ± 4.0	29.5 ± 3.8	0.05	28.3 ± 3.8
Glucose	[mmol/L]	8.5 ± 1.7	7.8 ± 1.1	0.05	5.5 ± 0.4
HbA1c	[%]	7.1 ± 0.7	6.8 ± 0.7	0.08	5.7 ± 0.3
GIR	[mg/kg·min]	2.7 ± 1.6	3.3 ± 2.2	0.03	5.4 ± 2.5
FFA	[mmol/L]	0.9 ± 0.4	0.9 ± 0.3	0.33	0.6 ± 0.2

Figure 1: Physical Performance

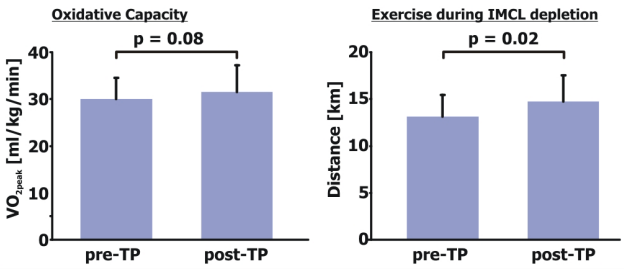


Figure 2: IMCL Levels

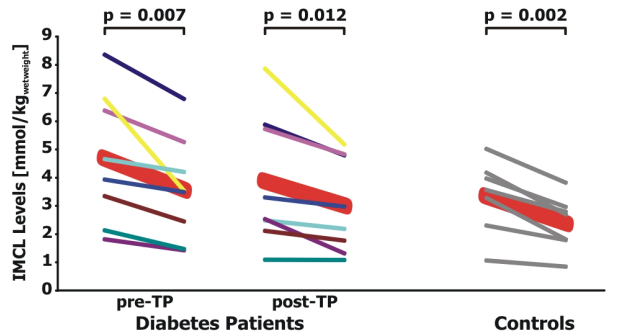
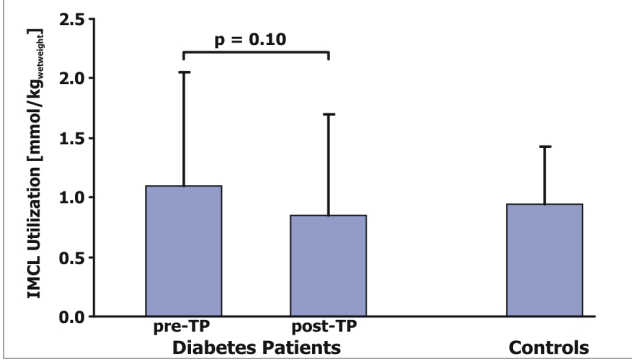


Figure 3: IMCL Utilization During 3h-Exercise



Results: Table 1 shows a summary of the clinical data. In addition, analysis of fasting blood parameters revealed that NIDDM patients – compared to the control group – had significantly higher levels of glucose ($p<0.001$), HbA1c ($p<0.001$), and free fatty acids (FFA, $p=0.03$) as well as a lower insulin sensitivity ($p=0.02$). Apart from FFA all parameters showed significant improvement, however values for glucose ($p<0.001$), HbA1c ($p=0.001$) and insulin sensitivity ($p=0.06$) remained different from the controls. Oxidative capacity was similar for patients and controls (30.0±4.5 vs. 30.8±5.7 ml/kg$_{bw}$, $p=0.77$) but tended to increase after the TP (to 31.5±5.7 ml/ kg$_{bw}$, $p=0.08$, see Figure 1). The distance covered during the exercise session increased after the TP (13.2±2.3 km to 14.8±2.8 km $p=0.02$) but was not different from the distance covered by the controls (14.9±4.3 km). Figure 2 shows that NIDDM patients and controls significantly depleted IMCL levels during the exercise session. The TP resulted in a significant reduction of $IMCL_{repleted}$ (4.7±2.3 vs. 3.9±2.3 mmol/kg$_{ww}$, $p = 0.05$). Before the TP $IMCL_{repleted}$ tended to be higher in NIDDM patients compared to controls (3.3±1.3 mmol/kg$_{ww}$, $p=0.09$) but not after TP ($p=0.29$). As shown in Figure 3 utilization of IMCL tended to be smaller after the TP (1.1±0.9 vs. 0.9±0.7 mmol/kg$_{ww}$) but was not different from the controls (1.0±0.5 mmol/kg$_{ww}$, $p = 0.71$ before and $p=0.80$ after TP).

Discussion: Evaluation of the clinical data clearly showed an improvement of metabolic parameters as well as an improved physical performance of the NIDDM patients after three month of a structured training program. Improved muscular insulin sensitivity was accompanied by an improvement of fasting blood glucose and HbA1c. However, these parameters remained significantly increased compared to the control group. The TP also affected the resting IMCL levels of the NIDDM patients leading to smaller values, thereby approaching the levels observed in the control group. It seems that the lower IMCL after TP led to a smaller IMCL utilization indistinguishable from the IMCL utilization of the control group, in keeping with prior observation.

Conclusions: This study demonstrates how much a 3-month structured training program has positive effects on the metabolic state and physical performance of NIDDM patients.

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