# Modification of skeletal muscle PGC-1a and UCP3 mRNAs after surgically induced body weight loss

**Project: 305**

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## Abstract

The aim of the present study was to investigate the metabolic modifications and insulin resistance accompanying surgical body weight loss as well as the regulation of genes which encode proteins involved in lipid oxidation such asUCP3 and PGC-1a.

**Research Methods and Procedures:**

Seventeen morbidly obese women were investigated before and 3 months after Roux-en-Y bypass, a restrictive surgical procedure, leading to a severe caloric restriction. 11 women accepted also to come at 12 months.
The group included 9 normoglycemic(NG) and 8 diabetic (DM) patients and the following parameters were measured : energy expenditure and substrate oxidation rate (indirect calorimetry); skeletal muscle mRNA expression of UCP3 and PGC-1a and insulin sensitivity (euglycemic hyperinsulinemic clamp).

**Results:**

The mean weight loss for the NG and DM patients was similar (41+/-2kg ). 50% of the total body weight loss occurred between 0 and 3 months(rapid phase) and 50% between 3 and 12 months post-surgery (slow phase). No difference was observed between the 2 groups.
As expected, pre-operative insulin sensitivity was significantly higher in the NG compared with the DM subjects (4.46 +/-0.68 versus 2.18 +/-0.55; $p < 0,01$). 12months after surgery insulin sensitivity significantly increased in both groups leading to normal blood glucose values.
Lipid oxidation increased significantly ($p < 0.05$) at 12months in the NG group, but not in the DG group.
Circulating free fatty acids (FFA) remained stable in both groups and were not affected by weight loss.
For both the NG and DM groups UCP3 mRNA values measured before surgery were similar (0.51+/-.078 NG and 0.68+/-0.17 DM ) and correlated positively with FFA values ($p<0.05$) in either groups. Surprisingly UCP3 mRNA values did not correlate with FFA levels at 3 and 12 months post surgery.
PGC-1a mRNA values (NG:0.99+/-0.33 and DM:0.87+/-0.17) increased significantly after body weight loss in both groups respectively ($p<0,05$, 12months after surgery : NG 1.52+/-0.44 vs DM: 1.45+/-0.34). We also observed a negative correlation between the difference in PGC-1 and blood insulin concentration at 3 months post-surgery ($p<0,0001$).

**Discussion:**

This study is the first to show an increase in skeletal muscle PGC-1a mRNA after surgically induced body weight loss in morbidly obese women. This increase in PGC-1a mRNA could be a contributing factor to the improved insulin sensitivity observed at 3 and 12months and supports previous observations in animal studies. In contrast UCP3 mRNA does not seem to be modified by surgically induced body weight loss except at 12months for the NG group. It is possible that the lack of upregulation in UCP3 in the DM subjects was in part a reason for their inability to increase lipid oxidation at 12 months post surgery. Further studies are required to better understand the relationship between PGC-1 and insulin sensitivity and between UCP3 and lipid oxidation following surgery induced weight loss.

**Key Words:** uncoupling proteins • PGC-1 • muscle biopsies • indirect calorimetry • morbid obesity