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Dietary and weight loss effects on human gut microbiome diversity and metabolism

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INTRODUCTION:

Recently an association of the gut microbiome and the human energy homeostasis has been shown, suggesting the gut microbiome as a possible target in obesity therapy. Additionally host metabolism is influenced by the gut microbiome, as the transfer of intestinal microbiota from lean donors to type 2 diabetes patients resulted in improved insulin sensitivity of the recipients. Further it has been shown, that nutritional load influences the overall microbial comunity in the gut. Therefore the impact of a multimodal obesity program including a VLCD (approx. 800 kcal/d) on gut microbiome an metabolism was examined.

METHODS

18 obese subjects underwent 3 months VLCD followed by 3 months of weight maintenance. A lean and an obese control group were included. The microbiome was characterized by performing high-throughput dual-indexed 16S rDNA amplicon sequencing.

Baseline characteristics of the study population

	Dietary Intervention (VLCD group)	Control Group I BMI<25	Control Group II BMI>30	P_{total}	P_1	P_2	P_3
gender (% female)	83.3	84.6	84.6	n.s.			
age (years)	47.0 (38.8, 54.5)	46.0 (37.5, 50.5)	50.0 (38.5, 54.0)	n.s.			
height (m)	1.70 (1.61, 1.73)	1.68 (1.64, 1.77)	1.68 (1.62, 1.73)	n.s.			
weight (kg)	123.8 (114.1, 143.5)	64.0 (56.7, 71.1)	123.5 (107.4, 138.1)	<0.001	<0.001	n.s.	<0.001
BMI (kg/m^2)	44.5 (38.8, 51.5)	22.4 (20.7, 24.0)	42.3 (35.2, 47.7)	<0.001	<0.001	n.s.	<0.001
fasting insulin (µU/ ml)	15.3 (10.4, 18.5)	8.6 (5.7, 10.3)	18.2 (12.7, 34.8)	<0.001	0.001	n.s.	<0.001
fasting glucose (mg/dl)	97.0 (90.5, 114.3)	87.0 (83.0, 110.0)	106.0 (89.0, 114.6)	n.s.			
HOMA-IR index	3.1 (2.6, 5.1)	1.9 (1.3, 2.5)	4.8 (3.1, 12.5)	<0.001	0.001	n.s.	<0.001

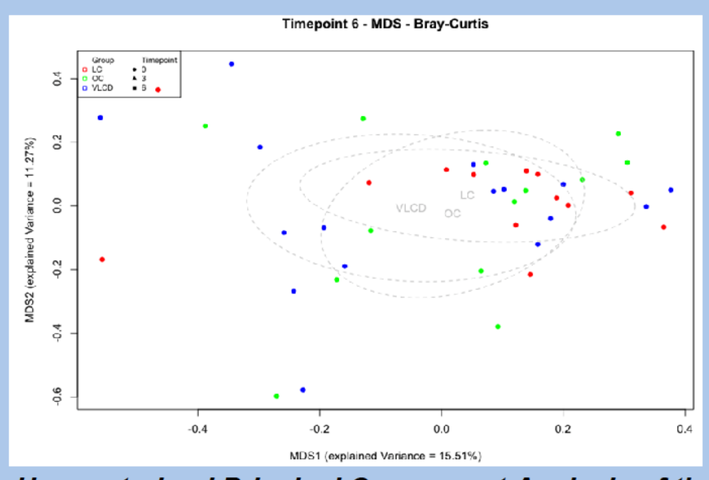
[1] median; 25th, 75th percentiles in parentheses (all such values)
p_{total} = p-value for overall comparison of the groups determined with Kruskal-Wallis with significance level set at p<0.05
p_{1-3} = p-values for comparison of the single groups performed by Mann Whitney U Test with p< 0.017 due to Bonferroni Adjustment : p_1= dietary intervention group vs. controls BMI< 25, p_2=dietary intervention group vs. controls BMI> 30, p_3 = controls BMI < 25 vs. controls BMI >30
Abbreviations: BMI= Body Mass Index; HOMA= Homeostasis Model Assessment index; n.s.= not significant

RESULTS:

Body weight and insulin sensitivity of the intervention group

	O months (beginning of the study)	3 months (end of VLCD)	6 months (end of weight maintenance)
weight (kg)	123.75** (114.08,102.25)[1]	102.30** (87.73,120.25)	99.35** (87.73-120.05)
HOMA-IR index	3.09* (2.61-5.14)	1.73* (1.03-3.70)	2.11 (1.51-3.87)

[1]median; 25th, 75th percentiles in parentheses (all such values)
Overall comparison was determined using Friedman test. Comparison between single points of measurements using Wilcoxon signed rank test: *p<0.01, **p≤0.001
Abbreviations: HOMA-IR= Homeostasis Model Assessment index

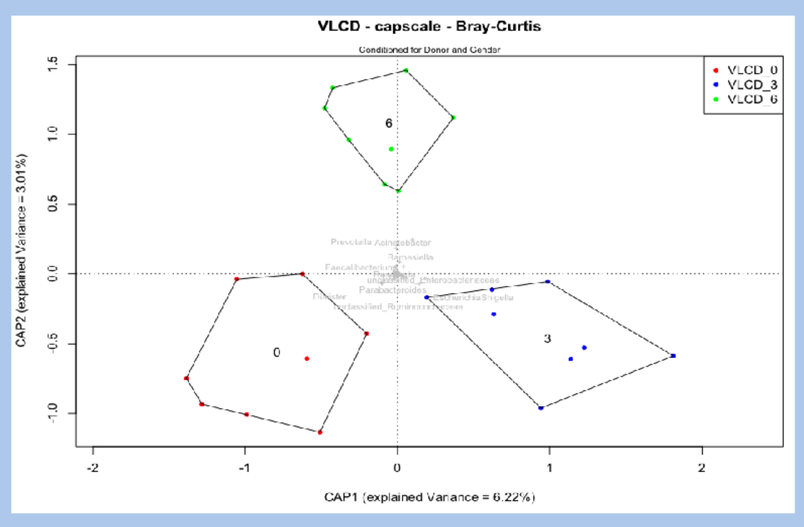


After weight maintenance no significant differences between the three study groups could be observed on phylum or genus level.

Unconstrained Principal Component Analysis of the intervention group and both control groups at the end of the study period.

Gut microbiome diversity

At baseline a significant difference in the Firmicutes/Bacteroidetes ratio between the lean control group and the obese intervention group could be observed (p=0.047).
The VLCD resulted in significant alterations in β-diversity from baseline to 3 months. The changes in diversity diminished during the weight maintenance phase, despite sustained reductions in body weight and sustained improvements of insulin sensitivity.



The first coordinate of the CAP explained 6.22% (p=0.048) of the variance in the microbiota due to the VLCD intervention.

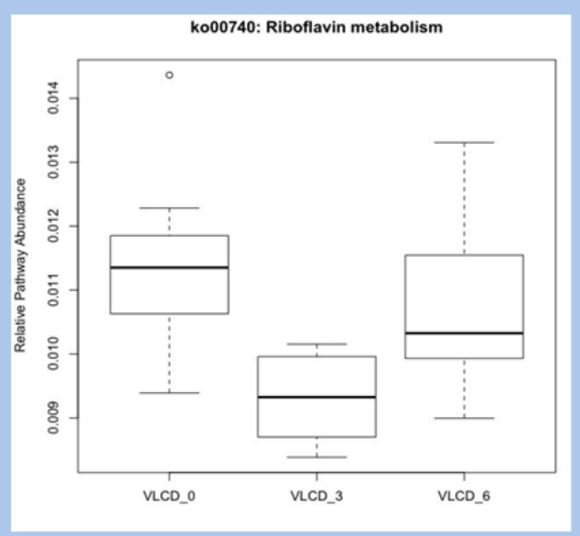
Constrained analysis of principal coordinates (CAP) of the dietary intervention group explaning variance in the microbiota. *Baseline (0 months)=0, VLCD intervention (3 months)=3, weight maintenance period (6 month)=6*

Defined species of the gut microbiome

Acinetobacter **represented an indicator species for the observed effect in microbiome diversity (IndVal=0.998; p=0.006).**

Bacterial metabolic changes

Metabolic analyses revealed nominal statistically significant alterations of the bacterial riboflavin pathway from baseline to 3 months (pnom=0.0078). During weight maintenance phase the changes diminished.



Relative abundance of the riboflavon pathway during the dietary intervention. *Baseline (0 months)=0, VLCD intervention (3 months)=3, weight maintenance period (6 month)=6*

CONCLUSION:

The present data show that in obese humans a VLCD is able to beneficially alter both gut microbiome diversity and metabolism, but also that these changes are not sustained during weight maintenance. This finding might suggest additional measures to target the microbiome during obesity programs.