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Swiss Federal Institute of Technology Zurich

Ernährungsbedingte Risikofaktoren für das metabolische Syndrom bei übergewichtigen Kindern

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Background

- Increasing childhood obesity worldwide
- Often: overweight children → overweight adults
- Link between obesity, subclinical inflammation, insulin resistance, hypertension and the metabolic syndrom in general in children and adults
- Little information on the association between dietary intake and inflammation, insulin resistance or hypertension

Aim of the study

To determine:

1. changes in childhood obesity over a period of 5 years
2. differences in dietary intake between normal weight and overweight children
3. the association between dietary intake and low grade inflammation, insulin resistance and high blood pressure, or overall the metabolic syndrome, in children

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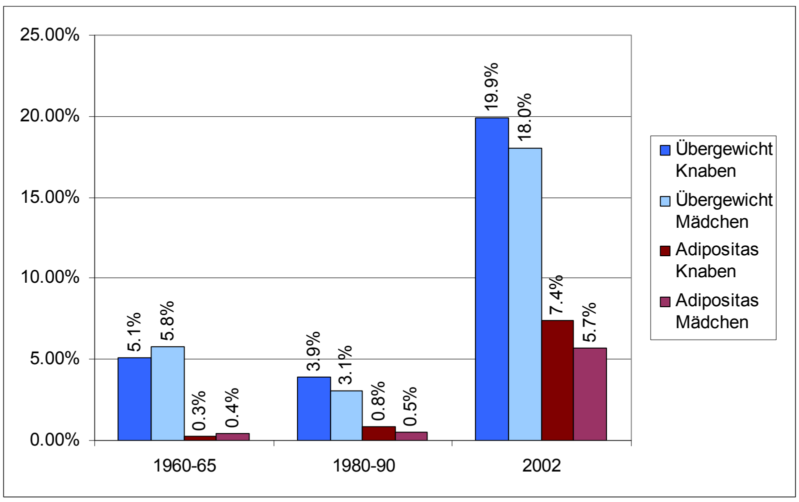
Prevalence of overweight and obesity in 6 to 12 year old children in Switzerland

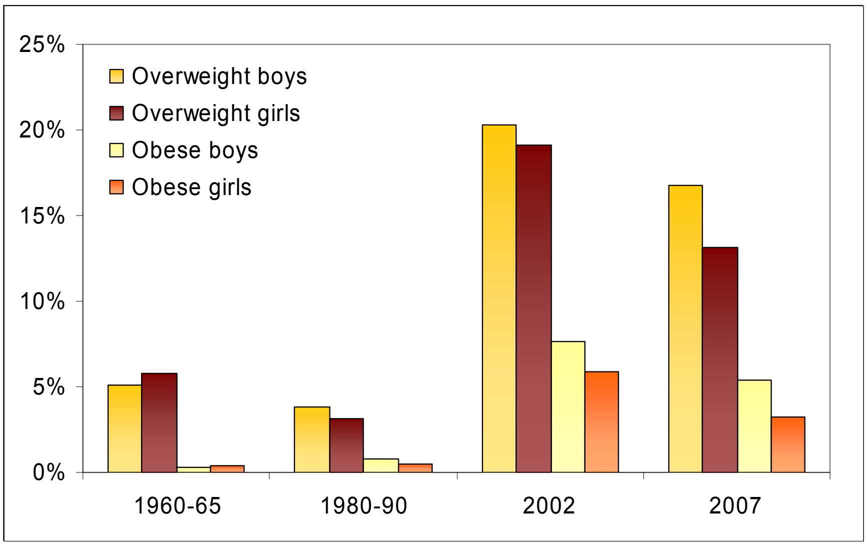


Zimmermann et al., SMW, 2004

Overweight in CH schoolchildren

- Sample:
  - 5 regions
  - 61 schools
  - 2303 children (age: 6 to 13 years)
- Measurments:
  - Weight and hight → BMI
  - Skinfold thiknesses → % body fat
  - Waistcircumference → ‚central obesity‘

Overweight in CH schoolchildren



Significant reduction of overweight in girls as well as obesity in both genders!

Aeberli et al., PHN, 2009

Dietary intake: Study design

- 156 children between 6 and 14 years
- Anthropometric measures: weight and height
- Dietary assessment (3 days)
- Physical activity questionnaire

Subject characteristics

	Normal weight		overweight	
	Girls	Boys	Girls	boys
n	31	43	34	34
Age (y)	9.46 ± 1.60[1]	9.64 ± 2.11	9.55 ± 1.50	9.81 ± 1.96
Height (m)	1.36 ± 0.11 [a]	1.38 ± 0.13 [a]	1.42 ± 0.11 [b]	1.43 ± 0.11 [a,b]
Weight (kg)	30.55 ± 6.79 [a]	31.35 ± 9.01 [a]	46.12 ± 11.76 [b]	47.27 ± 12.48 [b]
BMI	16.21 ± 1.60 [a]	16.12 ± 1.87 [a]	22.26 ± 2.81 [b]	22.65 ± 2.85 [b]

[1] mean ± SD (all such values)

Means not sharing a common superscript letter are significantly different from each other at $p<0.05$ (independent samples t-test).

Aeberli et al., SMW, 2007

Dietary assessment: Results

	normal weight		overweight	
	girls	boys	girls	boys
n	31	43	34	34
Energy intake (kcal)	1754 ± 317 [1,a]	1964 ± 373 [b]	1908 ± 289 [b]	1950 ± 286 [a,b]
Fat intake (g)	72.1 ± 16.0 [a]	80.7 ± 19.2 [b]	79.8 ± 21.0 [a]	79.4 ± 13.6 [a,b]
% energy as fat	36.1 ± 3.4	36.3 ± 5.3	36.5 ± 6.1	36.1 ± 4.8
Protein intake (g)	52.8 ± 11.7 [a]	60.8 ± 12.4 [b]	63.5 ± 12.3 [c]	66.6 ± 11.9 [c]
% energy as protein	12.3 ± 2.3 [a]	12.6 ± 2.1 [a]	13.5 ± 2.3 [b]	13.9 ± 1.9 [b]
Carbohydrate intake (g) [2]	222.9 ± 44.0 [a]	247.8 ± 57.0 [b]	233.5 ± 38.9 [a]	241.6 ± 47.4 [a,b]
% energy as carboh.	51.5 ± 4.5	51.0 ± 5.7	50.0 ± 7.3	50.0 ± 4.4
Fiber (g)	17.6 ± 4.6	17.3 ± 4.6	16.0 ± 3.5	16.1 ± 4.9
Dairy products g/d	260.2 ± 124.0 [a]	319.2 ± 197.3 [a,b]	350.0 ± 213.2 [b]	321.7 ± 196.4 [a,b]
Meat products g/d	45.5 ± 32.7 [a]	71.8 ± 39.7 [b]	78.5 ± 52.5 [b,c]	97.3 ± 44.5 [c]

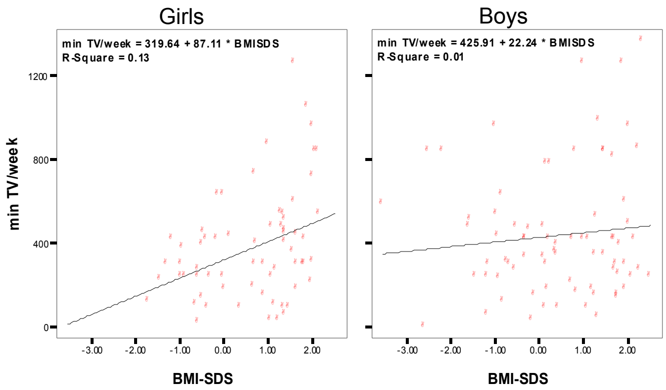
Aeberli et al., SMW, 2007

Dietary assessment: Results

- Energy intake: nw ♀ < ow ♀
- Protein intake: nw < ow (ob 16% > nw)
- Carbohydrate and Fat intake: no difference
- Meat intake: nw < ow (ob 85% > nw)
- Intake of dairy products: nw ♀ < ow ♀

Physical activity

- Organized physical activity: no differences
- TV/Computer: nw < ow



Aeberli et al., SMW, 2007

Metabolic aspects: Study design:

- 6 to 14 year old children:
  - 33 normal weight
  - 19 overweight
  - 27 obese
- BMI, W/H ratio, Body Fat%, blood pressure
- Fasting blood sampel
- Nutritional assessment (3 days)

Laboratory analysis

Insulin (→ RIA)
Glucose (→ Reflotron)
HDL-cholesterol (→ Hitachi)
LDL-cholesterol (→ Hitachi)
Triglycerides (→ Hitachi)
LDL-size (→ Gel electrophoresis)

RBP4 (→ ELISA)
TTR (→ELISA)
Serum retinol (→ HPLC)

CRP (→ Immulite)
IL-6 (→ ELISA)
Leptin (→ ELISA)
TNF-α (→ Immulite)
Resistin (→ ELISA)
Adiponectin (→ ELISA)
aP2 (→ ELISA)

Basic data of the children

	Normal weight	**Overweight**	**Obese**
n	33	19	27
Age (y)	10.1 ± 2.1[1]	10.1 ± 2.1	10.3 ± 1.9
Gender ratio (m/f)	20/13	8/11	14/13
BMI	15.9 ± 1.8	21.4 ± 2.4[2]	25.1 ± 2.62[2, 3]
Body fat %	19.9 ± 4.9	32.4 ± 5.8[2]	39.1 ± 5.2[2, 3]
W/H ratio	0.79 ± 0.03	0.82 ± 0.04	0.90 ± 0.06[2, 3]

1 mean ± SD (all such values)
2 significant difference compared to normal weight group ($p<0.05$) (ANOVA, post hoc Bonferroni)
3 significant difference compared to overweight group ($p<0.05$) (ANOVA, post hoc Bonferroni)

Data analysis with emphasis on five different aspects

- low grade inflammation and dietary intake
- insulin resistance / hypertension and dietary intake
- aP2, insulin resistance and diet
- RBP4, insulin resistance and diet
- LDL particle size and fructose consumption

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Why is inflammation important

- Subclinical inflammation is often present in overweight and obese children and adolescents and is associated with factors of the metabolic syndrome
- Little data is available on dietary determinants of subclinical inflammation, especially in children

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Results subclinical inflammation

- Subclinical inflammation is present in overweight Swiss children
- Dietary intake may influence inflammation:
  - Not specific types of fat, but total fat intake predict subclinical inflammation
  - Meat intake predicts IL-6 and leptin but not CRP
  - Intake of antioxidant vitamins only predicts leptin

Aeberli et al., AJCN, 2006

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Components of the metabolic syndrome

- With increasing adiposity:
  - Increasing fasting insulin concentrations and decreasing Quantitative Insulin Sensitivity Check Index (QUICKI)
  - Increasing systolic and diastolic blood pressure
- Prehypertension or hypertension was diagnosed in 40% of the overweight and obese children

Aeberli et al., IJVNR, 2009

Dietary intake

- Prediction of fasting insulin and QUICKI in normal weight children by:
  - Energy
  - Total fat (g), saturated fat
  - Protein
  - Dairy products

- Prediction of SBP in all children by:
  - Total fat (g), saturated and monounsaturated fat

Aeberli et al., IJVNR, 2009

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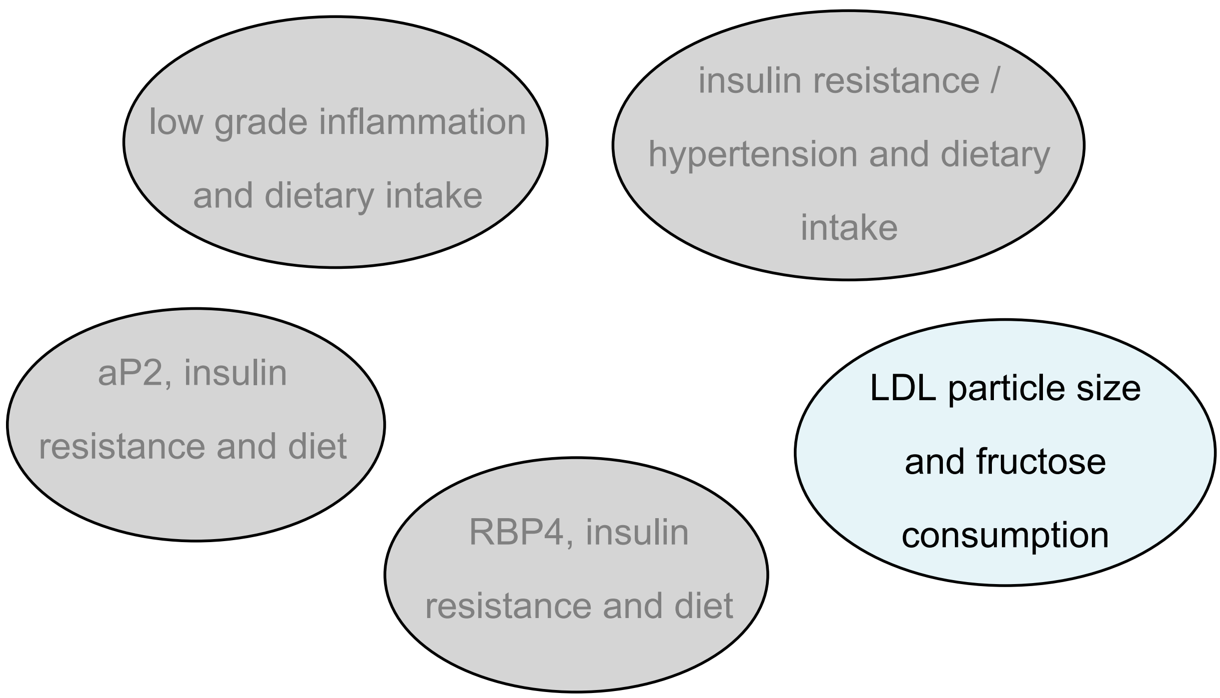


Why measure LDL size?

- Two different main patterns of LDL particles:
  Pattern A: large particles
  Pattern B: small, dense particles
- Small, dense LDL particles have been shown to be atherogenic
- Small, dense LDL particles are more prevalent in overweight/obese persons

LDL size and nutrition

- Very little data is available on dietary determinants of LDL particle size:
  - Increased total carbohydrate intake may lead to a reduction in LDL size
  - No data on specific types of carbohydrates or on the effect of other nutrients

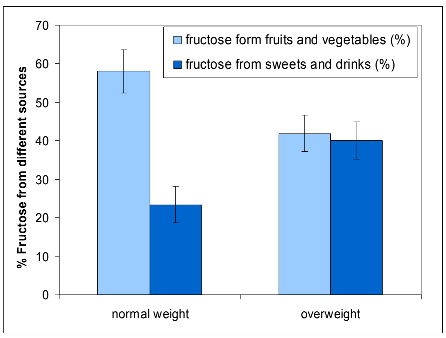
Results: LDL size and lipids

- In overweight children:
  - Plasma triglycerides increased ($p<0.001$)
  - HDL cholesterol decreased ($p=0.003$)
  - LDL particle size decreased ($p=0.005$)
- LDL particle size was inversely correlated to BMI-SDS ($p=0.007$), BF% ($p=0.002$) and W/H ratio ($p<0.001$)

Aeberli et al., AJCN, 2007

Results: Dietary factors

- Dietary factor predicting LDL size:
  - Total fructose intake ($p=0.024$)
- No correlation between fructose intake and any of the other lipid parameters
- More fructose from sweets and drinks in overweight children



Aeberli et al., AJCN, 2007

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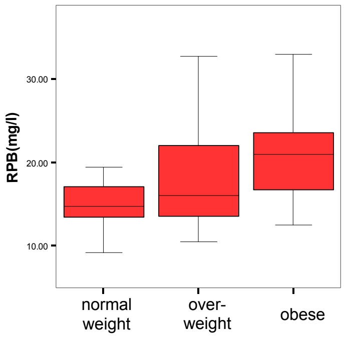
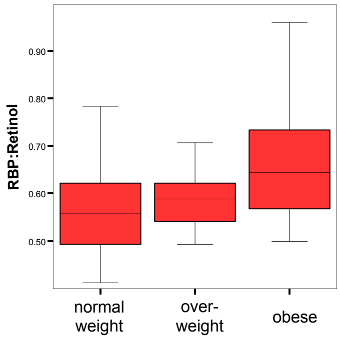
Retinol binding protein (RBP) 4 in the context of overweight and obesity?

- RBP4 has recently been identified as an adipokine
- In mice, RBP4 increases insulin resistance in the muscle and hepatic gluconeogenesis
- In humans the association of RBP4 with insulin resistance and obesity is less clear

RBP4 and adiposity

- BMI, BF% and W/H ratio predicted RBP4 and serum retinol independet of vit A intake, age and CRP





Aeberli et al., JCEM, 2007

RBP4 and the metabolic syndrome

- Independent of adiposity:
  - Significant correlation between RBP4 as well as RBP4/SR and serum triglycerides
  - Significant correlation of RBP4/SR with fasting insulin

Aeberli et al., JCEM, 2007

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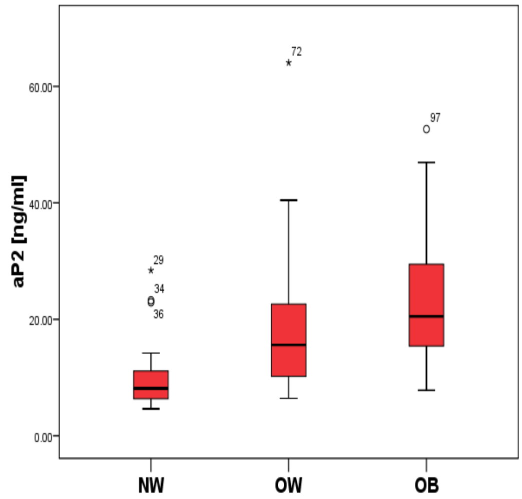
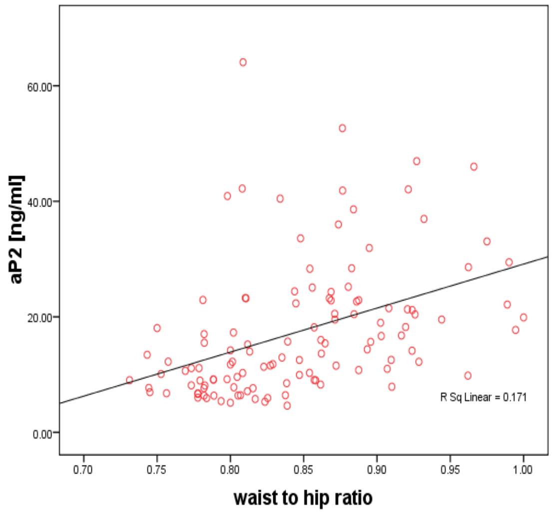
The adipocyte fatty acid binding protein aP2

- One of nine fatty acid binding proteins; expressed in adipocytes
- Transport of FA in and between cells; important in lipid signaling cascades
- Link between obesity, inflammation and the metabolic syndrome?
- Associations with insulin resistance, dyslipidemia and metabolic syndrome in adults

aP2 and obesity





→ aP2 is increased with total and central obesity!

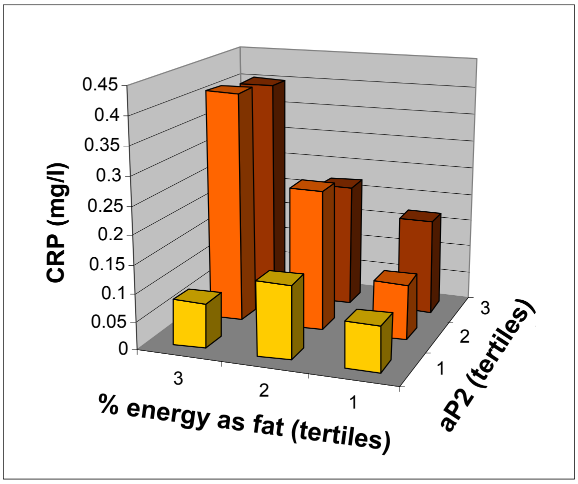
Aeberli et al., IJO, 2008

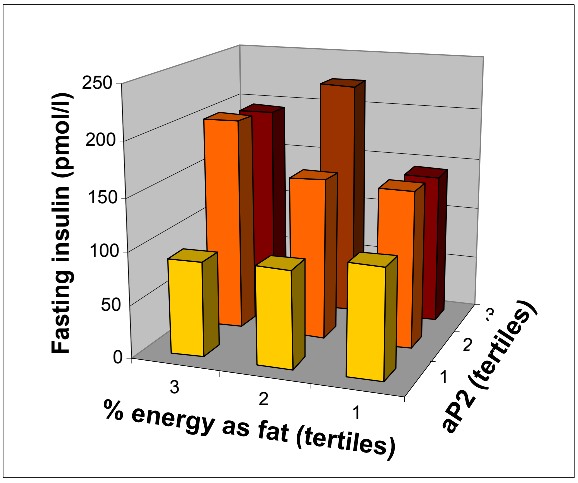
aP2, metabolic syndrome and diet

- aP2 and the metabolic syndrome:
  - Fasting insulin / QUICKI
  - Blood pressure
  - Serum triglycerides
  - Serum HDL- and LDL-cholesterol
  - Inflammation (CRP, leptin, IL-6)
- aP2 and dietary factors:
  - Fruits and vegetables, vitamins A, C and E

Aeberli et al., IJO, 2008

aP2, metabolic syndrome and diet





→ Differences in adipokines may be important for the effect of dietary changes on metabolic abnormalities

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Summary

- Decrease in prevalence of childhood overweight over 5 years
- Small differences in diatary intake between nw and ow children, physical activity may be just as important
- Dietary components are associated metabolic abnormalities
- Interactions between adipokines and dietary factors may be of importance

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