

Original

Social and behavioural aspects and their consequences in obese teenagers - importance of family's history

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Abstract

Objectives: Overweight, the metabolic syndrome and accompanying diseases are dramatically increasing problems. We investigated social and behavioral variables that influence overweight in adolescents and tested their influence on plasma markers related to diabetes and endothelial dysfunction.

Methods: 79 male adolescents were enrolled (age 13-17 years). Endothelial progenitor cells were counted by flow cytometry. Adiponectin and soluble E-selectin (sE-selectin) were determined by ELISA.

Results: Body weight differs significantly if the family's history was positive for arterial hypertension ($p < 0.001$), diabetes ($p < 0.001$), hypercholesterolemia ($p < 0.001$), and coronary artery disease (CAD, $p < 0.01$). The hours of physical activity represent a predictor of BMI in linear regression analysis ($p < 0.001$; $R^2 = 0.195$). Markers for endothelial damage are altered in adolescents with positive family history for hyperlipidemia and CAD.

Conclusion: The family's history is an important variable influencing the body weight of teenagers. Via obesity and independently, it influences the early development of endothelial damage. It might serve to detect teenagers at risk for appropriate intervention.

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Key words: Adolescents. Overweight. BMI. Exercise. EPC. Soluble E-selectin. Adiponectin.

ASPECTOS SOCIALES Y CONDUCTUALES Y SUS CONSECUENCIAS EN ADOLESCENTES OBESOS - IMPORTANCIA DE LOS ANTECEDENTES FAMILIARES

Resumen

Objetivos: El sobrepeso, el síndrome metabólico y sus enfermedades asociadas son problemas que están aumentando de forma notable. Investigamos las variables sociales y conductuales que influyen en el sobrepeso en adolescentes y probamos su influencia sobre los marcadores plasmáticos relacionados con la diabetes y la disfunción endotelial.

Métodos: Se reclutaron 79 adolescentes varones (edad 13-17 años). Se contaron las células progenitoras endoteliales con citometría de flujo. Se determinaron la adiponectina y la selectina-e soluble (selectina-s) mediante ELISA.

Resultados: El peso corporal difiere significativamente si los antecedentes familiares son positivos para hipertensión arterial ($p < 0,001$), diabetes ($p < 0,001$), hipercolesterolemia ($p < 0,001$) y arteriopatía coronaria (APC, $p < 0,01$). Las horas de actividad física representan un predictor del IMC en el análisis de regresión lineal ($p < 0,001$; $r^2 = 0,195$). Los marcadores de lesión endotelial están alterados en los adolescentes con unos antecedentes familiares positivos para hiperlipidemia y APC.

Conclusión: Los antecedentes familiares son una variable importante que influye en el peso corporal de los adolescentes. A través de la obesidad y de forma independiente, influye en el desarrollo precoz de lesión endotelial. Podría servir para detectar a los adolescentes con riesgo para realizar una intervención apropiada.

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Palabras clave: Adolescentes. Sobrepeso. IMC. Ejercicio. EPC. Selectina-e soluble. Adiponectina.

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Introduction

Overweight and the metabolic syndrome are dramatically increasing problems, especially in children and adolescents.¹ The prevalence of overweight in children and adolescents has tripled in recent decades and related health costs have nearly quadrupled.²

Childhood overweight significantly increases the risk for adult obesity and for greater severity of obesity in adulthood.³ More than 60 percent of overweight children between 5 and 10 years of age in Louisiana (USA), have at least one risk factor for cardiovascular disease, such as elevated blood pressure or serum insulin levels or dyslipidemia, and 25 percent have more than one risk factor.⁴ In German overweight and obese children and adolescents there is a significant association between weight, carotid vessel wall changes and blood pressure, as well as various other metabolic parameters.⁵ Type 2 diabetes mellitus now accounts for up to 45 percent of all newly diagnosed diabetes in pediatric patients⁶ and is frequently asymptomatic.⁷

Recently,⁸ we were able to show that overweight in adolescence has a negative impact on different parameters that are important for the future cardiovascular prognosis, including adiponectin, an early marker for beginning insulin resistance, soluble E-selectin (sE-selectin), a marker for endothelial damage, and the number of Endothelial Progenitor Cells (EPCs).

EPCs are bone marrow-derived pluripotent circulating vascular progenitor cells, capable to contribute to reendothelialization and neovascularization processes,⁹ as well as a biomarker of cardiovascular risk.¹⁰⁻¹² Circulating EPCs home to sites of ischemia and vascular injury as a repair mechanism to denuded or dysfunctional endothelium.¹³ Indeed, numerical and functional impairment of EPCs has been linked to endothelial dysfunction,^{10,14} increased atherosclerotic disease risk¹⁵ and greater cardiovascular¹¹ and cerebrovascular¹⁶ morbidity and mortality.

In older ages and after exposure to risk factors lower bioavailability, limited mobilization and impaired function of EPCs have been suggested to contribute etiologically to vascular dysfunction and disease.^{8,17-19} Physical activity increases the production of EPCs, an effect that could potentially underlie exercise-related beneficial effects on cardiovascular diseases.²⁰ In adults, several case-controlled studies and evaluations in patient series have demonstrated inverse associations, for example, between EPC number and diabetes,²¹ hypertension,²² family history for coronary artery disease (CAD),²¹ Another factor influencing EPCs, especially their lifetime, is insulin resistance.²³

Insulin resistance is the condition in which normal amounts of insulin are inadequate to produce an appropriate insulin response from fat, muscle or liver cells. A surrogate parameter to monitor an altered insulin sensitivity or insulin resistance is adiponectin. Adiponectin is an adipokine that is specifically and abundantly

expressed in adipose tissue and directly sensitizes the body to insulin. A decrease in plasma adiponectin levels precedes the onset of diabetes, reveals the state of decreased insulin sensitivity, and correlates inversely with insulin resistance.²⁴

Another approach to determine the early cardiovascular risk profile is to measure the vascular activation via soluble markers of endothelial damage. SE-selectin, which correlates with functional and morphological changes of the vessel wall in obese teenagers,²⁵ is such a marker for endothelial damage and activation.

Many factors influence the development of obesity in adolescents. This includes increased intake of high-fat foods, sweetened soft drinks, fruit and vegetable intake, and sport habits for example as modifiable determinants and families' medical history as fixed variable. Teenagers' education might be a factor influenced by external institutions.²⁶

This study examines the impact of a variety of social and behavioral variables on the development of obesity and the influence on different markers for cardiovascular risk stratification, endothelial damage and insulin resistance independent of the teenagers' body weight.

Methods

Study subjects

79 male, Caucasian adolescents (aged 13-17 years) living in Germany were studied. Subjects and their parents gave informed consent and protocols were approved by the University's ethics committee in accordance with the Helsinki Declaration.

Individuals were recruited in the region of Jena, Germany. For all participants the following parameters were recorded in one consultation: age, height, weight, BMI, hip circumference, waist circumference, hip/waist-ratio, heart rate, and blood pressure (systolic and diastolic). Family history (first-degree relatives) for different diseases was recorded. Renal cystic diseases and chronic renal failure were summarized as renal diseases. Coronary artery disease, heart failure, sudden cardiac death and need of pacemaker or arrhythmias were summarized as cardiac diseases. Social and behavioural attributes and habits were recorded first with a questionnaire and additionally with a personal interview. Any sign of acute disease was an exclusion criterion.

Routine laboratory

Standard serum parameters were obtained from the Department of Clinical Chemistry at the University Hospital Jena (Friedrich-Schiller-University): creatinin (umol/l), cholesterol (mmol/l), high-density lipoprotein (mmol/l), low-density lipoprotein (mmol/l), triglycerides (mmol/l), lipoprotein (a)

Table I
Baseline characteristics of the study population. In parts published before⁸

N	79	Creatinin, (umol/l)	79.8 ± 11.5
Age, y	15.2 ± 1.1	Cholesterol (mmol/l)	4.0 ± 0.8
Male gender, n (%)	79 (100)	high-density lipoprotein (mmol/l)	1.2 ± 0.2
Body height, cm	175 ± 8	low-density lipoprotein (mmol/l)	2.5 ± 0.8
Weight, kg	79.5 ± 22.3	LDL / HDL ratio	2.2 ± 0.9
BMI	26.1 ± 7.1	triglycerides (mmol/l)	1.0 ± 0.6
Waist circumference, cm	85.6 ± 16.8	lipoprotein (a) (mg/l)	222.9 ± 287.8
Hip circumference, cm	95.6 ± 16.7	high sensitive CRP (mg/l)	1.65 ± 2.9
WHR	0.89 ± 0.05	HbA(1c), %	5.1 ± 0.3
Heart rate at rest, 1/min	78 ± 15	leukocytes, Gpt/l	6.5 ± 1.7
Systolic blood pressure, mmHg	130 ± 17	erythrocytes, Tpt/l	5.2 ± 0.3
Diastolic blood pressure, mmHg	72 ± 8	lymphocytes, Gpt/l	2.3 ± 0.6
		Smokers, %	15.9%

(mg/l), high sensitive CRP (mg/l) (hsCRP), automated white blood count differential.

Circulating EPC Number

EPCs were identified as described before.⁸ Briefly, flow cytometry counted cells coexpressing 3 characteristic antigens: the hematopoietic progenitor cell marker CD34, the immature hematopoietic progenitor cell marker CD133, and the endothelial cell receptor VEGFR2 (Vascular endothelial growth factor receptor 2, also known as kinase domain receptor, KDR). Peripheral blood mononuclear cells (PBMC) were stained with fluorescein-isothiocyanate (FITC)-conjugated anti-human CD34 monoclonal antibody (mAb) (BD Biosciences), phycoerythrin (PE)-conjugated anti-human CD133 mAb (Milteny Biotec) and biotin-conjugated monoclonal Anti-VEGFR2 (Sigma, Sigma-Aldrich). Control isotype- and species-matched antibodies were used (BD Biosciences). Streptavidin-PerCP (BD Biosciences) was used for secondary labeling. Stained cells were resuspended and analyzed by 3-color flow cytometry (FACS Calibur-Becton Dickinson). The cytometer was set to acquire 500.000 events in the lymphocyte gate, in accordance with a technique used by other investigators.²⁷ Analyses were performed using the Cell Quest software program (Version 5.2, BD Biosciences). EPCs were then calculated to cells/ml.

Enzyme Linked Immunosorbent Assays (ELISAs)

The quantitative determination of human Adiponectin and sE-selectin concentrations were analyzed using the quantitative sandwich enzyme immunoassay technique (R&D Systems, Wiesbaden, Germany) according to the manufacturers' instructions.

Statistical Analysis

Data are expressed as mean ± standard deviation (SD). To describe the relationship between two variables, without making any assumptions about the frequency distribution, non-parametric rank correlation coefficient (Spearman's) was calculated. Comparisons with nominal parameters having more than two values were calculated with one-way ANOVA. For assessment of linear relationship single linear regression analysis was performed. Statistical significance was assumed if a null hypothesis could be rejected at $p \leq 0.05$. All statistical analyses were performed with SPSS, version 12.0 (SPSS Inc.).

Results

The baseline characteristics of the 79 subjects are summarized in table I. Families' medical history is summarized in table II, behavioral characteristics are shown in table III, as well as the social background in table IV.

Table II
Frequency of different kind of diseases in the families' history

Families' medical history, positive for:

Hypertension, (%)	43%
Diabetes mellitus (%)	38%
Hypercholesterolemia (%)	19%
Renal diseases (%)	13%
Cardiac death (%)	14%
Cardiac diseases, including CAD (%)	32%

Table III
Behavioral aspects in daily life of adolescents focusing on sport, smoking and alimentation habits

<i>Sport</i>	
Regular sport activity (%)	72
Hours per week of sport, h (Range)	5.3 ± 3,6 (0-12h)
Regularity per week (% of total population)	
1x	13.6
2-3x	44.1
4-6x	30.5
Daily	11.9
Duration per sport activity (% of total population)	
Less than 1 hour	26.3
1-2 hours	42.1
More than 2 hours	31.6
Assessment of the own fitness (%)	
1 (best)	10.1
2	27.8
3	26.6
4	27.8
5	6.3
6 (worst)	1.3
<i>Smoking</i>	
Regular smoker (%)	15.9%
Average consumed cigarettes per smoker (1/day)	4.8
<i>Alimentation</i>	
Warm food at home or in school (%)	
Never	0
1-2 x/week	13.9
3-5 x/week	8.8
> 5 x/week	77.2
Parents pay attention to the child's alimentation (%)	82.0
Parents prepare food for the morning school break every day (%)	53.2
Sweets consumption frequently (%)	41.0
Fruit consumption frequently (%)	63.3
Soft drink consumption frequently (%)	20.7

Body mass index

The BMI in teenagers was higher if the families' history was positive for: hypertension ($p < 0.001$), diabetes mellitus ($p < 0.001$), hypercholesterolemia ($p < 0.001$), renal diseases ($p = 0.024$) and coronary heart disease ($p < 0.01$, fig. 1). Hyperuricemia and sudden cardiac death groups did not differ.

Adolescents without a regular sport activity had a higher BMI ($p < 0.001$). Linear regression analysis revealed the association between hours of sport activity per week as a predictor of BMI ($p < 0.001$; R^2 : 0.195, fig. 2). However, the duration of the single sport activity and the regularity of the sport did not have an impact on BMI. The self assessment as surrogate parameter of the fitness was also in strong inverse linear correlation with the BMI ($p < 0.001$; R^2 : 0.427). Smokers and Non-smokers did not differ in BMI.

Table IV
Teenager's family's characteristics

Number of siblings (%)	
0 x	26.6
1 x	45.6
2 x	20.2
> 2 x	7.6
Father has university degree (%)	20.0
Mother has university degree (%)	24.4
Educational level of attended secondary school (%)	
High	31.6
Middle	51.9
Low	16.5

Regarding the alimentation no differences were seen between groups regarding the frequency of warm food at home, the assessment whether parents pay attention to the child's alimentation, the regularity of food prepared for school's break, and the consumption of sweets, fruits, and soft drinks.

The number of siblings had no impact on body weight. Child's BMI did differ between the groups with mothers having a university degree or not ($p = 0.021$), favouring lower BMI in higher educated mothers. This did not apply for fathers with or without university degree. The educational level of the attended school correlated with BMI favoring teenagers on schools with higher educational status for lower BMI ($p = 0.011$).

Adiponectin, soluble E-selectin and EPCs

None of the families' medical history correlated with the level of adiponectin. Also, none of the alimentation and social factors had impact on adiponectin. Teenagers with families history for coronary artery disease ($p = 0.038$) and hyperlipidemia ($p = 0.035$) had significantly higher sE-selectin levels. No other factor regarding sport, smoking, alimentation habits and social aspects had significant impact on sE-selectin. All investigated factors did not influence EPC numbers in the teenager population.

Discussion

This study examined the effect of social and behavioral variables on the body weight and markers for cardiovascular risk stratification, including also details of the family's history for different diseases. Overall, data showed a strong impact of family's history, sport activity, and educational level on the BMI. Surprisingly the evaluation of alimentation habits revealed no significant impact. Generally, the influence of social, educational and behavioral aspects seem to have nearly no impact on early endothelial dysfunction, beginning diabetes and EPC mobilization, independently from

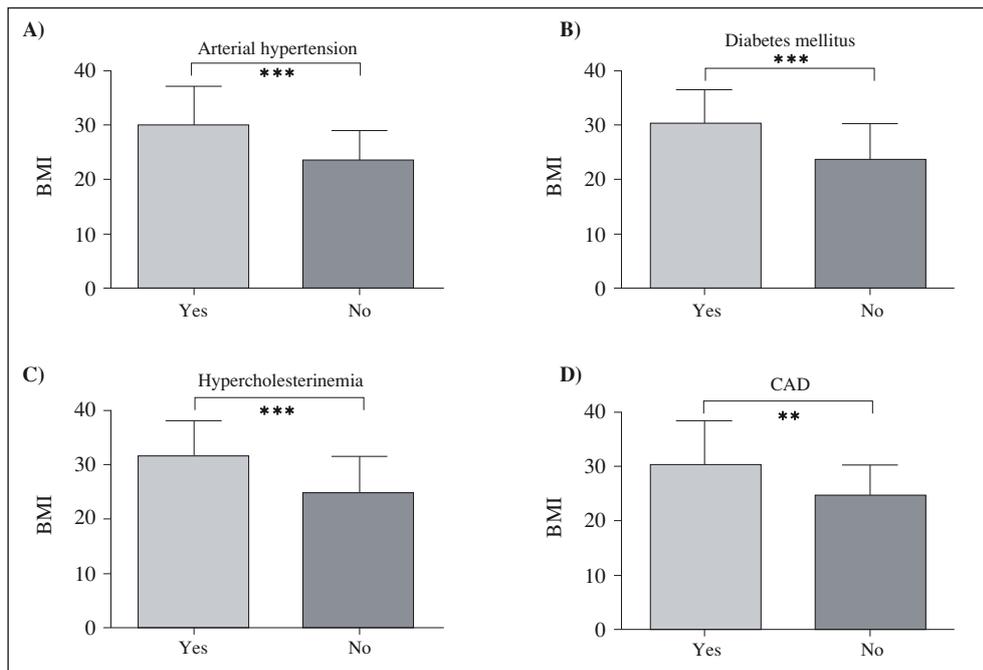


Fig. 1.—BMI shows significant differences while grouping adolescents according to the families history for arterial hypertension (A), diabetes mellitus (B), hypercholesterolemia (C), and coronary artery disease (D). ***: significant at the $p < 0.001$ level; **: significant at the $p < 0.01$ level. CAD: coronary artery disease.

body weight and including obese and normal weight teenagers. However, the family's history influences the upcoming early disease stages in early life. The impact of these factors via body weight is described elsewhere.⁸

Obesity and influencing factors

The development of obesity in young ages was associated with a positive family history for hypertension, diabetes mellitus, hypercholesterolemia, renal diseases, and coronary heart disease. This is in accordance with findings of other investigators: Robinson and coauthors found that children whose family members had arterial hypertension had increased BMI compared with children without family history of hypertension.²⁸ A study on male teenagers showed that young subjects with familiar history of diabetes have a higher prevalence of overweight and central obesity compared to other groups.²⁹ However, controversial data exists investigating the BMI of children with family members with CAD: two studies reported negative results,^{30,31} whereas our data is in accordance with a polish study.³² Furthermore a higher BMI, as well as higher incidence of hypertension and hypercholesterolemia, is reported in adolescents and young adults in first-degree relatives of dialysis patients.³³ No data of this kind exists for hypercholesterolemia. This data underlines the importance of the family's history. Although this variable can not be influenced it is an easy tool to detect children at risk in order to intervene with lifestyle modifications.

A lifestyle characterized by excessive inactivity (particularly television viewing) is thought to cause

obesity in children and adolescents. Physical activity was inversely associated with prospective BMI change in girls, and media time (watching television or videos, playing video or computer games) was directly associated with BMI change in both sexes. Moreover, low aerobic fitness predicts increased adiposity in black and white children.³⁴ We detected the hours of physical activity per week as predictor of BMI pointing out the importance of regular and frequent sport.

The diet has also drawn interest as an important determinant of weight gain. Especially the easy availability of fast food and sweetened soft-drinks and fur-

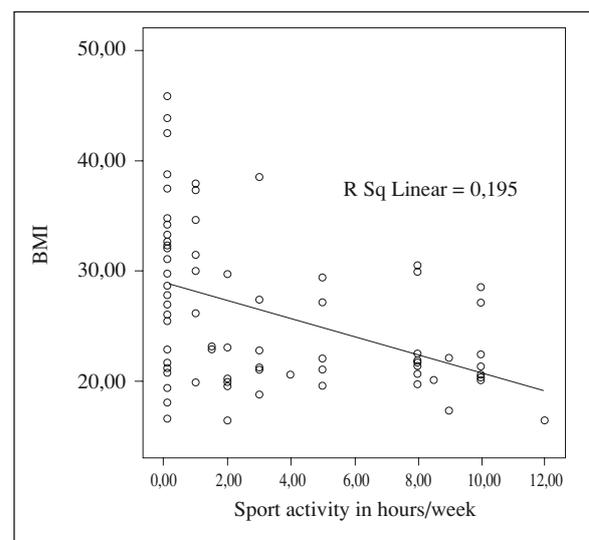


Fig. 2.—Linear regression analysis reveals the sport activity (hours/week) as independent predictor of the body weight ($p < 0.001$; $R^2: 0.195$).

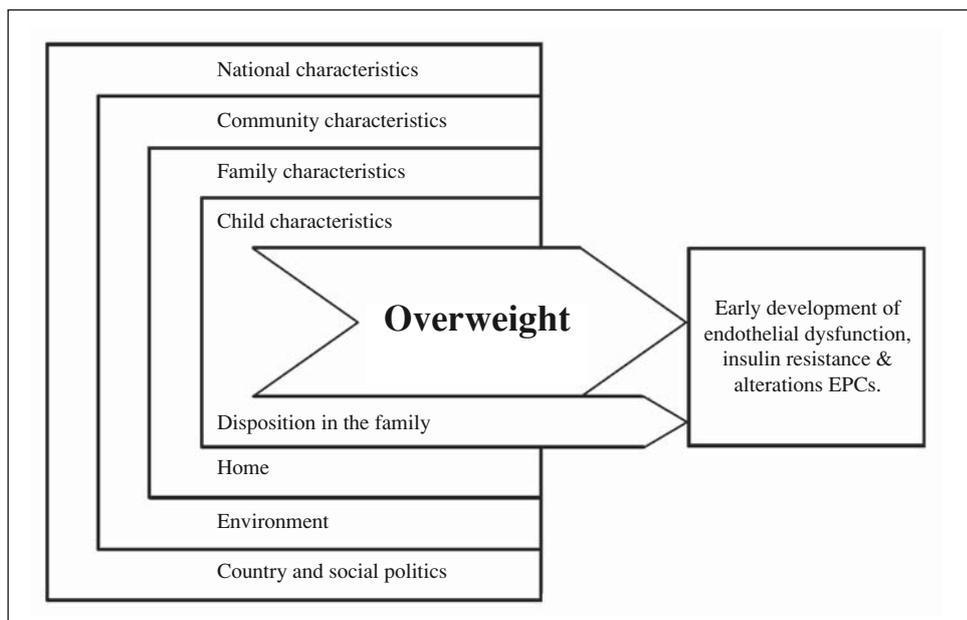


Fig. 3.—Influences on adolescence overweight and their influence on future maladies; a framework modified from Hawkins et al.⁴⁰.

thermore the related consumption of far too much calories results in disproportional weight rise.³⁴ Our study population did not differ in BMI grouping according to the diet habits. That might be explained by the fact that the study took place in central Germany, former eastern part. All enrolled teenagers went still to school in which a common lunch is provided with big impact on the answers of our questionnaire.

Low income, education, and time resources, as well as poor neighborhoods have all been shown to contribute to the higher risk of being overweight in adolescence. Indeed the risk of having a BMI above the 85th percentile was associated with low parental educational level.³⁵ The own intellectual capacity is of importance, as well: A lower IQ score in childhood is associated with obesity and weight gain in adolescence and adulthood.³⁶ Our findings support this observation. An overview on the dimensions influencing overweight in adolescence is given in figure 3.

Obese adolescents and cardiovascular risk factors

This disproportionate weight gain in adolescence is associated with many consequences both in younger ages and in adulthood. Especially the epidemic of obesity in younger ages has led to a parallel rise in the prevalence of pediatric forms of diabetes, insulin resistance, endothelial dysfunction.³⁷ Various consequences of overweight in young life include altered blood pressure, elevated hsCRP, increased HbA(1c), lower high-density lipoprotein, as well as decreased adiponectin, higher sE-selectin and early activated EPC as surrogate parameters for insulin resistance, endothelial damage, respectively. We described these associations earlier elsewhere.⁸

Influences independent of overweight

The majority of social and behavioral factors did not influence the markers of beginning insulin resistance or endothelial dysfunction. This indicates the overwhelming importance of overweight. A big part of future problems, in our case the beginning insulin resistance, the endothelial damage and the altered EPCs, is mediated by overweight. Only the family's history of different kinds of illnesses comes to evidence. This is known for the investigated illnesses like diabetes and CAD, proved by studies determining the concordance of identical twins and the aggregation in some families. Recently Kelly et al. observed a decline in insulin sensitivity and β -cell function during pubertal growth, which was influenced by a maternal family history of diabetes. These effects became stronger as children became older.³⁸ Whittacker et al. described a significant correlation between healthy parents and their offspring and CAD parents and their offspring, suggesting that EPC number is, at least in part, genetically regulated.³⁹

Conclusions

A significant family's history, especially for hypertension, hypercholesterolemia, diabetes and CAD, has an impact on adolescents' body weight and also on future diseases – mediated via obesity and independently, as well. Since the families history is not influenceable it could serve to detect teenagers at risk for early intervention during overproportional weight gain. The majority of the development of early disease stages, including insulin resistance and endothelial damage, is a consequence of obesity. Furthermore our study con-

firms especially the importance of physical activity for the prevention of adolescence overweight.

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