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BODY SIZE AND PHYSICAL ACTIVITY

Epidemiological studies on children and young adults

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First we form habits, then they form us.
Conquer your bad habits or they will conquer you.

Robert Gilbert

ABSTRACT

The overall aim of this thesis was to increase the knowledge about different aspects of body size and physical activity among Swedish children and young adults. Specific aims were: (i) to investigate how BMI-distributions (BMI=Body Mass Index) have changed among Swedish children over a 12 year period, (ii) to study effects of pre- and postnatal growth on body size and body composition in adolescence, (iii) to study associations between parents' and children's physical activity, and (iv) to investigate genetic contributions to physical activity behavior.

The study of changes in BMI-distributions was based on a comparison of two population-based cohorts; one of 3,650 children born in 1973-75 and a one of 2,591 children born in 1985-87 - the COMPASS study. The comparison showed marked differences in the BMI-distributions from 5-6 years of age with higher BMI-values in the younger cohort. No differences were observed for the children at 2-5 years of age. Differences started to appear at the 25th percentile and became increasingly pronounced in the upper parts of the distributions, i.e. the heavy children became heavier over the 12 year period.

The COMPASS study was also used for the study of associations of pre- and postnatal growth with body size and body composition at age 15. Prenatal growth, measured with birth weight z-score, was positively associated with BMI, fat free mass, fat mass and waist circumference. For one unit increase in birth weight z-score, fat free mass increased 1.66 kg among boys and 1.05 kg among girls. Further, there was a positive relation between prenatal growth and fat mass as percentage of total body mass among boys, but not among girls. Postnatal growth, measured by change in weight z-score during first year of life, showed strong, positive associations with all measures of body composition in adolescence. For one unit increase in weight z-score during first year of life, fat free mass increased 2.30 kg among boys and 1.64 kg among girls. Postnatal growth had stronger effect than prenatal growth on all measures of body composition.

The study of associations between parents' and children's physical activity was based on the PITCH study. The study population comprised 1,124 12-year-old children and their parents. Parents' physical activity was strongly associated with their children's participation in sport and vigorous activities. With two parents active in sport the odds ratio for their children to participate in sport was 3.9 (95% CI, 2.2; 6.9) (girls) and 8.8 (4.3; 18.0) (boys) compared with having two inactive parents.

The Swedish Young Male Twins Study was used to investigate the contribution of genetic factors to physical activity behavior. The study population comprised 2,044 male twins born 1973-1979. There were moderate to high genetic contributions to physical activity. Heritability estimates were in the range of 0.40 to 0.65, depending on physical activity dimension. Only additive genetic and non-shared environmental factors seemed to be of importance for the variation in physical activity in this young adult male population.

LIST OF PUBLICATIONS

This thesis is based on the following papers which will be referred to in the text by their Roman numerals.

I. Eriksson M, Rasmussen F & Nordqvist T. Changes in shape and location of BMI distributions of Swedish children. Acta Paediatrica 2005;94:1558-1565.

II. Eriksson M, Tynelius P & Rasmussen F. Associations of birth weight and growth during infancy with body composition at age 15 – the COMPASS study. Submitted.

III. Eriksson M, Nordqvist T & Rasmussen F. Associations between parents' and 12-y-old children's sport and vigorous activity: the role of athletic competence. Submitted.

IV. Eriksson M, Rasmussen F & Tynelius P. Genetic factors in physical activity and the equal environment assumption – The Swedish Young Male Twins Study. Behavior Genetics 2006;36:238-47.

CONTENTS

LIST OF ABBREVIATIONS

BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CI	Confidence Interval
DLW	Doubly Labeled Water
DXA	Dual X-ray Absorptiometry
EE	Energy Expenditure
EEA	Equal Environment Assumption
FFM	Fat Free Mass
FM	Fat Mass
MBR	Medical Birth Register
MET	Metabolic Equivalent
OR	Odds Ratio
RMR	Resting Metabolic Rate
SD	Standard Deviation
SEM	Structural Equation Modeling
WC	Waist Circumference

1 INTRODUCTION

Epidemiology is concerned with studying the distribution and determinants of disease frequency and is often regarded as the core science of public health.[1] Body size, overweight and obesity have been under study by epidemiologists and other health professionals for a long time. Obesity is a chronic condition with an excessive accumulation of body fat.[2] Overweight and obesity are developed due to positive energy balance, i.e. when energy intake is larger than energy expenditure (EE) for a prolonged period of time. There is substantial evidence that obesity is a strong risk factor for several chronic diseases, e.g. cardiovascular disease and type II diabetes.[3] Research has also shown social consequences of obesity, as lower attained education,[4] lower household income[5] and increased risk of disability pension.[6] Obesity in childhood and adolescence also has adverse effects on adult health.[7,8] In a long term follow up, adults who were obese in adolescence had higher risk of all-cause mortality compared with normal weight subjects, regardless of their current body size.[8] In addition, childhood obesity has short term consequences such as strong relations to cardiovascular risk factors, type II diabetes and psychological problems.[9,10] Obese children have lower self esteem compared with normal weight children.[11-13] Further, body size at birth, in childhood and adolescence track into adulthood.[14-18] In a study from the US, 77% of obese children were also obese as adults,[19] emphasizing the importance of establishing a healthy body size in childhood that can be maintained throughout life.

Physical activity is defined as “any bodily movement produced by skeletal muscles that results in energy expenditure”.[20] Leisure time physical activity represents a broad category of activities performed outside work. Exercise is a subset of physical activity and is defined as “physical activity that is planned, structured, repetitive and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective”.[20] Occupational physical activity is associated with activity performed during the daily work. Epidemiological research on physical activity started in the 1950’s with Jeremy N. Morris investigations of coronary heart disease among bus drivers and conductors in London. He found that conductors, who were more on their feet, had lower rates of coronary heart disease than bus drivers who were entirely sedentary.[21] Since then research has discovered that physical activity is beneficial for preventing obesity and chronic disease, for enhancing initial weight loss and prevention of weight regain.[22-27] Among adults, physical activity is inversely related to all-cause mortality,[28-31] cardiovascular disease,[30,31] type II diabetes,[32-34] osteoporosis,[35,36] some cancers,[30,37] depression[38] and obesity.[39] Further, recent reviews indicate that physical activity in obesity treatment, in addition to dietary restrictions, has favorable effects on body composition, i.e. prevents loss of fat free mass (FFM).[40] In childhood and adolescence, physical activity is related to self esteem, obesity, cardiovascular risk factors and bone density.[41-43] Physically active children have shown greater increase in FFM, including both muscle mass and bone mass, and less accumulation of fat mass (FM) compared with physically inactive children.[44-46] A recent study of 5,500 children found strong inverse associations between physical activity and FM and a smaller positive association with FFM.[47] Among obese children physical activity has additional beneficial effects on insulin resistance and physical fitness.[48]

Several studies have shown that physical activity declines with age from adolescence and that males are more active across the life span.[49-52] Further, they tend to engage in more vigorous physical activity than females.[51,53] On the contrary, an extensive review found no association between age and physical activity among children 3-12 years of age.[50] There are, however, some indications of tracking of physical activity from childhood into adulthood, even though it seems to be low or moderate.[54,55] Some studies suggest that specific aspects of childhood physical activity, such as participation in vigorous and organized sport activities and physical activity skills in adolescence, may be more strongly related to adult physical activity.[56,57]

Physical fitness, in contrast to the behavior physical activity, is "a set of attributes that people have or achieve" which relate to the ability to perform physical activities.[20] Physical fitness can be divided into health-related and skill-related fitness. The health-related fitness is more important from a public health point of view and consists of five components; a morphological component, including body composition, a cardio-respiratory component, a muscular component, a motor component and a metabolic component.[58] Physical activity, physical fitness and health are related in a complex way. Physical activity can influence physical fitness which in turn can modify physical activity levels. Both physical activity and physical fitness are related to health in a reciprocal manner.[58] Also physical fitness declines with age among adults, which is, to some extent, an effect of the general physiological decline that occurs as we grow old. There is, however, some support that this decline can be attenuated with physical activity throughout life.[59] Physical fitness tracks better from childhood and adolescence into adulthood compared with physical activity.[55,60,61]

TRENDS IN BODY SIZE AND PHYSICAL ACTIVITY

The prevalence of obesity has been increasing world wide for the last decades and is a large contributor to the global burden of disease.[62] Also among children the prevalence has increased greatly.[63] There is research from the US suggesting that the childhood obesity of today will have a marked impact on the economy, through health care cost and loss of productivity, when these obese children become adults.[64,65] In Sweden, the prevalence of obesity increased 3.5 times among conscripts between 1971 and 1995,[66] and during the last two decades it has doubled among adults and was approximately 10% among both men and women in 2002/2003.[67] Among ten year old children in the western part of Sweden, there was a fourfold increase in obesity between 1990 and 2000/2001, resulting in a prevalence of 2.9% in the latter survey.[68] A study of 10-16 year olds found a 2.5 fold increase in the prevalence of overweight and obesity combined between 1987 and 2001, resulting in a prevalence of 20%.[69] The corresponding figure was 18.2% for boys and 14.5% for girls among 15-year old adolescents in Stockholm 2000/2001.[70] Recent research has shown that the increase in obesity, based on increase in Body Mass Index (BMI, weight in kg divided by height in m^2), among children during the last decades may underestimate the increase in FM. Contemporary children have much higher FM, lower FFM and higher waist circumference (WC), indicating more abdominal fat accumulation,[71] compared with children a few decades ago. Children are fatter today than in the recent past.[72,73] This is further indicated by several studies that have shown that the increase in prevalence of overweight and obesity during the last decades largely is a result of changes in the upper end of the BMI-distribution.[69,74-76] A recent study have reported that the median BMI increased among Swedish adolescents between 1987 and 2001 and that the most pronounced changes occurred in the upper part of the BMI-distribution.[69]

Total physical activity have decreased among adults in industrialized countries during the last decades, with the greatest declines in occupational physical activity,[77-80] walking/cycling[78,79] and, among women, household activity.[78] However, leisure time physical activity and participation in organized sports have increased during the same period.[77,80,81] Also among children and adolescents in industrialized countries, leisure time physical activity and participation in organized sports has increased and today constitutes a large proportion of the total physical activity.[82-85] The proportion of Swedish adolescents that engaged in organized sports at least twice a week increased from less than 20% among girls and around 40% among boys in 1968 to approximately 45% (girls) and 57% (boys) in 2001. However, concurrently the non-organized physical activity decreased and the proportion inactive adolescents, i.e. those who did not engage in sport activities during leisure time, increased from less than 10% in 1968 to approximately 20% in 2001.[83,86] In accordance with adults, walking and cycling have decreased among children and adolescents in the US, Great Britain and Australia.[82,87] In an Australian study from 2001, reported over 90% of 9-13 year old children that they never cycled to school.[87] However, in a Swedish study of 15 year olds from 2000/2001, 73.6% reported that they walked or cycled to school every day, while 4.7% reported that they never walked or cycled at all.[70]

Physical fitness has declined among Swedish children and adolescents during the last decades. 16-year old girls and boys performed less well in sit-up-, run-walk- and bench-press-tests in 1995 than in 1974.[88] Similar declines were observed in a comparison of cardio-respiratory and neuro-muscular fitness among children and adolescents in 1987 and 2001.[89]

PHYSICAL ACTIVITY RECOMMENDATIONS

Physical activity recommendations have changed over the years from being more directed towards improving and maintaining physical fitness components and thus recommending more vigorous activities, to the recognition that also physical activity of moderate intensity has health benefits.[90] There are several recommendations in the literature with different health and fitness implications. This has been illustrated by a "physical activity pie" which combines recommendations for health and recommendation for fitness.[91] Today most recommendations for health among adults are in accordance with the Swedish one, freely translated: "All individuals should, preferably every day, be physically active for minimum 30 minutes. The intensity should be at least moderate, e.g. brisk walking."[92] This corresponds to an energy expenditure of about 1000 kcal/week. According to a consensus in 2003, there is need for 45-60 minutes of moderate physical activity every day for prevention of weight gain and 60-90 minutes for prevention of weight regain after weight loss.[39]

There are several physical activity recommendations for children and adolescents. Most of them recommend 30-60 minutes of moderate to vigorous exercise every day.[93,94] For pre pubertal children the Swedish recommendation is at least 60 minutes of moderate physical activity every day.[92]

CONCEPTUAL FRAMEWORK

Several theories and models have been developed to understand the factors and processes which affect the balance between energy intake and energy expenditure. According to ecological models changes in a persons characteristics are influenced by both personal and environmental factors.[95] Examples of factors influencing energy intake and expenditure at the individual level are sex, age and genetic factors. The environmental factors can be separated into several levels, for example the interpersonal level, which consists of e.g. family and peers, and the larger environment, represented by the physical environment, e.g. day care facilities and schools, policies, cultural and social norms and values. Figure 1 presents a framework for how obesity may develop among children.

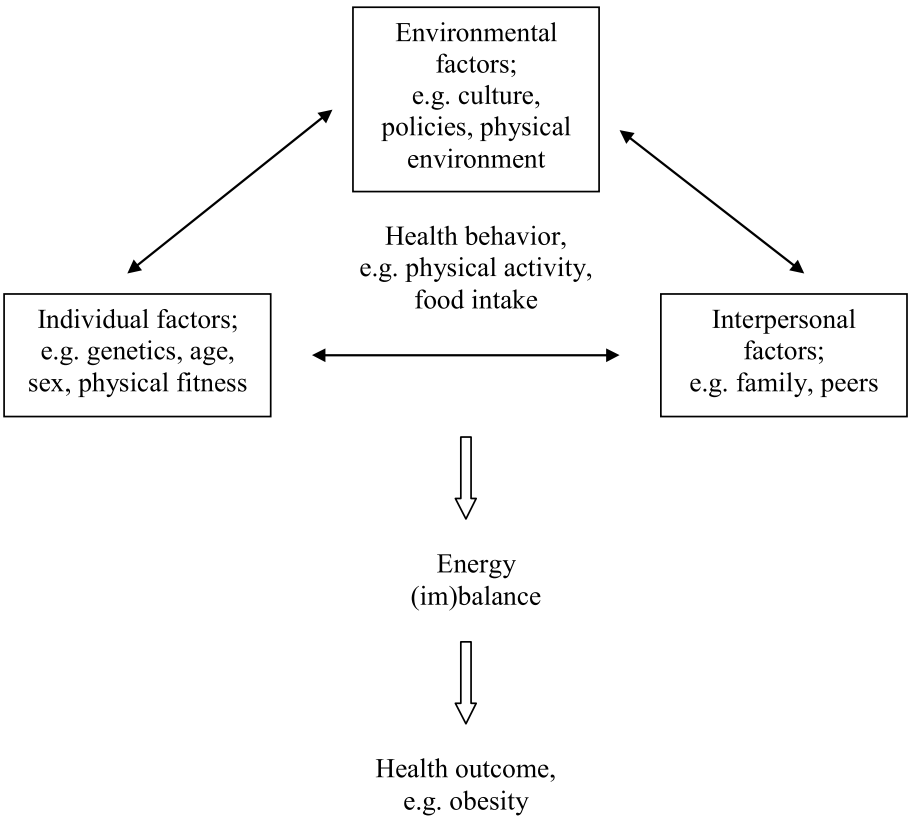


Figure 1. A framework based on ecological models for understanding the development of obesity.[95]

This thesis studies different aspects on the individual and interpersonal levels but also discusses possible effects of factors in the larger environment. Main focus is on the energy expenditure side of the energy balance equation.

Pre- and postnatal growth

Many studies have shown associations of prenatal and postnatal growth with chronic disease in adult life.[96-99] Prenatal growth is most often measured by birth weight for gestational age or ponderal index (PI, weight in kg divided by length in m^3) in epidemiological studies. Birth weight and PI are positively associated with BMI in adulthood.[100,101] However, birth weight is inversely associated with a number of chronic diseases, e.g. coronary heart disease, hypertension and type II diabetes.[98] This contradiction could partly be explained by, as an increasing number of studies indicate, that birth weight to a larger extent is associated with FFM compared with FM.[102-106] Further, research has shown that birth weight is inversely related to central obesity, which is associated with the chronic diseases mentioned above.[100,101]

Postnatal growth is often measured as change in weight, length or BMI standard deviation (SD) score, so called z-score, in early childhood. Z-scores are derived by transforming the observations into a normal distribution with mean 0 and SD 1. A change in e.g. weight z-score over a specific time period indicates a relative change in weight in relation to all other subjects in the study population. Others, however, suggest use of original data.[107] The postnatal period is defined diversely in the literature, from a few weeks after birth to several years into childhood. Postnatal growth has shown positive associations with BMI later in life.[108,109] Most of the few studies that have investigated relations between postnatal growth and body composition later in life have found positive associations between increased weight gain in early childhood and both FFM and FM later in childhood or early adult life.[103,110-112] It has been suggested that intrauterine growth restricted children, i.e. children born small for gestational age, compensate with rapid weight gain in infancy, so called "catch-up growth" and that these children have an increased risk of obesity and chronic disease in adulthood.[99,113]

Genetic factors

Genetic factors also affect our health, body size and composition, and also energy intake and energy expenditure.[114-117] Heritability of BMI, i.e. the proportion of the phenotypic variation that is explained by genetic factors, is around 0.70.[114,118] Also the specific compartments of body composition, FM and FFM, are affected by genetic factors. FFM has shown heritability estimates of around 0.60 among adults[117] and over 0.80 among children.[119] Also FM is highly influenced by genetic factors, with heritability estimates up to over 0.80 among children and adolescents[119,120] and around 0.60 among adults.[117]

Furthermore, genetic factors influence different human behaviors, e.g. eating behaviour.[121] Genes also seem to be important for physical activity. Studies on physical activity behavior have shown genetic contributions in the wide range of no effect to 0.83 depending on age, gender, study design, studied physical activity dimension and methods used for assessing physical activity.[119,122-133] Participation in sport and vigorous activities has shown very heterogeneous results regarding the impact of genetic factors. Boomsma et al found high heritability on sport participation among adolescent twins,[124] while Perusse et al did not find any genetic effect on participation in exercise activities in a family study.[123] Lauderdale et al found higher influence of genetic factors on activities of higher intensity compared with moderate physical activity.[126] More recent studies have found heritability between 0.35-0.83 for sport participation.[127,134] One study of adolescent twins found that genetic effects started to appear at age 17-18 and then increased into early adulthood, whereas the effect of shared environmental factors largely accounted for the variation in sport participation in younger years.[134] This is in accordance with a study that did not find any genetic effect on physical activity level among young children.[119]

Familial environmental factors

Factors related to the familial environment have also been associated with both energy intake and physical activity.[50,135] Several studies have shown that factors such as role modeling and parental support are important for children's and adolescents' physical activity.[50,136-138] A French study of 3,000 12 year olds showed that children were more likely to participate in sport activities when both parents practiced sport than when none of the parents were active, with an odds ratio (OR) of 1.97 (95% CI, 1.4; 2.8) for boys and 1.56 (1.2; 2.1) for girls.[138] A large study of US adolescents found positive, but weak, associations of family cohesion, parent-child communication and parental engagement with adolescent moderate and vigorous physical activity (ORs between 1.09-1.25).[139] The literature on the influence of parental physical activity is, however, inconclusive.[140]

Psychological factors

As mentioned above, both obesity and physical activity is related to psychological factors.[12,38,42] Self-esteem and self-efficacy, defined as the individual's belief in his/her ability to maintain or change specific behaviors and overcome barriers,[141] is associated with physical activity among children and adolescents.[42,139,142,143] Athletic competence, which has been conceptualized as a dimension of self-esteem, measures children's perceptions of their own ability in sport and outdoor activities.[144] Athletic competence in relation to physical activity has only been investigated in a few studies, with inconclusive results.[143,145-147] One study found that physical activity skills in adolescence were related to physical activity level in adulthood.[56] Overweight adolescents have few characteristics that are positively correlated with physical activity compared with normal weight adolescents. For example, overweight adolescents have reported lower self-efficacy and less support from the family in being physically active.[148,149]

ASSESSING BODY SIZE AND BODY COMPOSITION

In epidemiological studies, body size, overweight and obesity is most often measured by BMI. According to WHO criteria, overweight among adults is defined as BMI ≥25 and obesity as BMI ≥30.[2] BMI has shown to be a relatively good estimate of excess body fatness and is considered a valid measurement in epidemiological studies.[150] Among children under 18 years of age, there are age and sex-specific cutoff points, developed by the International Obesity Task Force.[151] There are other definitions used in the literature, as different BMI-percentiles of specified reference populations.[152,153] However, there are critique against the use of BMI to define overweight and obesity in childhood and adolescence. The BMI cutoff points have high specificity, i.e. very few normal weight children are diagnosed as overweight or obese, but only modest sensitivity, i.e. many overweight or obese children are misclassified as normal weight.[154,155] Even though BMI correlates fairy well with body fatness in children, at least among children in the upper part of BMI-distributions,[154,156,157] estimating the prevalence of obesity in children is complicated since children grow. After an initial increase in BMI during infancy, BMI decreases to the age of 6-7 years. Hereafter BMI increases throughout adolescence and young adulthood. Increase in BMI after 6-7 years of age is due to both FM and, to a larger extent, FFM.[158] FFM follow the growth patterns of height and weight and before the adolescent growth spurt there are only small differences in FFM/height between boys and girls. In young adulthood, however, men have about 0.36 kg FFM for every cm of stature, whereas women have only 0.26 kg. The difference is mainly due to higher stature and muscle mass among men. Total FM increases during the first 2-3 years of life and is then stable through the preschool years. Subsequently, FM increases more in girls than in boys and in young adulthood women have 1.5 times the FM of men. Relative fatness, i.e. %FM, increases rapidly during infancy and then declines during early childhood. Girls have slightly higher %FM than boys from infancy, but after 5-6 years of age they have a consistently greater %FM, which increases gradually until adulthood. Boys' %FM increases until the adolescent growth spurt, when it start to decline.[44]

There are several methods to assess FFM and FM. Computed tomography, dual X-ray absorptiometry (DXA) and densitometry are accurate methods but not feasible in epidemiological studies due to high cost and high requirements for study participants' cooperation and time. Bioelectrical impedance analysis (BIA) is a less precise, but non-invasive method, easy to use in a field setting and is relatively inexpensive. There is need for control of hydration status, physical activity and food intake before measurement, which has been shown to affect impedance measurements. With these factors under control, BIA was found to be a valid method to estimate body composition among children and adolescents in a cross-validation study against hydrostatic weighing and deuterium dilution.[159]

Other anthropometric measures to assess body size and body fatness are WC and skinfold thickness. As mentioned above, WC is a measure of central fat accumulation, which is related to chronic disease in adulthood.[160] Skinfold thickness measured by calipers at several body locations estimates subcutaneous fat.

ASSESSING PHYSICAL ACTIVITY

In quantifying physical activity, the intensity, duration, frequency and type of activity are of interest. Activities are often divided into categories of intensity defined by MET-values (metabolic equivalents), which are based on rate of energy expenditure. One MET is defined as the energy needed at rest - equivalent to the resting metabolic rate (RMR) - which corresponds to approximately 3.5 ml oxygen per kg body weight and minute, or one kcal per body weight and hour for an average adult person.[161,162] The duration is the length of the time period when performing the activity, frequency is the number of occasions per unit of time, e.g. per day, week or month, performing the activity, and examples of different types of activities are strength training and aerobic activities. The methods to assess physical activity can be divided into three types; criterion methods, objective methods and subjective methods.

Criterion methods

Criterion methods are the most valid and reliable methods against which all other methods to assess physical activity should be validated. There are three criterion methods; indirect calorimetry, the doubly labeled water method (DLW) and direct observation. Indirect calorimetry measures EE from oxygen consumption and carbon dioxide production. It is, however, only applicable in laboratory settings and thus not suitable for field studies. DLW is on the other hand possible to use in field studies. A dose of two stable isotopes (^{2}H and ^{18}O) are administered orally and the isotopes distribute themselves in equilibrium with body water. ^{2}H eliminates from the body as water ($^{2}H_2O$) and ^{18}O as water ($H_2{}^{18}O$) and carbon dioxide ($C^{18}O_2$). The difference in elimination rates of the isotopes provide a measure of carbon dioxide production and therefore of EE. However, DLW can only measure total EE and consequently not make a distinction between physical activity EE, RMR and the thermal effect of feeding. Further, it is an expensive method not suitable for large scale epidemiological studies. Another issue regarding these two methods is that EE is not equivalent to physical activity, but an effect of it. The third criterion method, which is considered the most appropriate criterion method for physical activity behavior, is direct observation. It is a direct behavioral observation of the motor activities and the essence is to classify physical activity behaviors into categories that can be quantified. Drawbacks of this method is potential influence of the observer on the study subjects' behavior and that it is very time consuming and therefore not suitable in large scale studies.[163,164]

Objective methods

There are several objective methods to assess physical activity. Heart rate monitors rely on the linear relationship between heart rate and oxygen consumption. This relationship is, however, not so robust at the low end of the physical activity spectrum, where heart rate is affected by other factors such as stress, caffeine intake and some medications. Motion sensors as pedometers and accelerometers register body movement. Pedometers register movement in the vertical direction and are used to count steps over a period of time. Accelerometers register movements in more than one plane and are therefore more accurate in estimating EE than pedometers. However, none of these devices can be used in water or can register movements in cycling or the upper body.[163]

Subjective methods

Subjective methods include questionnaires, activity diaries and interviews. These methods are appealing because of their low costs and ease to apply, and are widely used in epidemiological studies. They are however relying on self-report and are subject to over- and underestimation of physical activity levels.[165] Caution should especially be taken when using subjective methods among children, since their cognitive ability is lower compared with adults and therefore have lower capability to recall frequencies, intensities and duration of activities.[166,167] Accordingly, validation studies among children have shown very different results, mainly depending on age.[164] Validation studies among adults have shown that questionnaires in general might be valid to classify populations into categories of physical activity behavior, e.g. low , moderate and high active, but they are not appropriate to quantify EE at the individual level.[168]

ASSESSING GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO PHYSICAL ACTIVITY

The twin study design provides a useful tool for examining the contributions of genetic and environmental factors to complex human traits as physical activity. Twin studies make it possible to decompose the total phenotypic variance into genetic and environmental components and are based on differences in similarity between monozygotic (MZ) twins, who are genetically identical, and dizygotic (DZ) twins, who share, on average, 50% of their segregating genes. Additive and dominance genetic effects have an expected correlation of 1.0 within MZ pairs and 0.50 and 0.25 within DZ pairs, respectively. Higher degree of resemblance among MZ twins is assumed to be due to genetic factors. To illustrate, if the intra-pair correlation is 1.0 among MZ twins and 0.5 among DZ twins, the trait would be influenced only by additive genetic factors. If the phenotypic correlation is lower within MZ pairs, for example 0.8, and the corresponding value among DZ pairs is half of that, i.e. 0.4, there is an influence of environmental factors unique to the individual in addition to the additive genetic effect. If the DZ correlation is greater than half of the MZ correlation, e.g. 0.5 (DZ) vs. 0.8 (MZ), there is an additional effect of environmental factors shared by the twin pair. If instead the DZ correlation is less than half of the MZ correlation there is presence of dominance genetic effects.[169]

The twin analyses performed in this thesis work is relying on several assumptions. One assumption is absence of gene-environment interaction, i.e. the influence of genetic and environmental factors on the studied trait does not go beyond the additive action of these factors. The possible effect of gene-environment interaction is estimated as part of the additive genetic component to the extent the environmental factors interacting with the genes are shared within the twin pairs. To the extent such environmental factors are not shared between twin pairs, the unique environmental component will absorb the effect. Furthermore, an assumption of random mating is made. Positive phenotypic assortment may increase DZ correlations and thus inflate the estimates of shared environmental variance and reduce the genetic variance. Another central assumption is the equal environment assumption (EEA), i.e. that MZ and DZ with-in pair correlations is equal in environmental factors of etiological importance for the studied trait. If MZ correlations are higher in these environmental factors, the genetic effect will be overestimated.[170]

2 AIMS OF THE THESIS

The overall purpose of this thesis was to increase the knowledge on different aspects of body size and physical activity among Swedish children and young adults.

Specific aims were:

- to investigate how BMI-distributions have changed among Swedish children during a 12 year period
- to study effects of pre- and postnatal growth on body size and body composition in adolescence
- to study associations between parents' and children's physical activity
- to study the contribution of genetic and environmental factors to physical activity

3 MATERIAL AND METHODS

THE COMPASS STUDY (PAPER I AND II)

The papers examining changes in BMI-distributions and effects of pre- and postnatal growth on body size and body composition were based on the COMPASS study – Community-based study of physical activity, life style and self-esteem in Swedish school children. The COMPASS study was initiated in 2000 with the purpose to survey physical activity, eating habits, self-esteem and body size among Swedish adolescents. The children in the study were residents of a geographically well-defined area of Stockholm County with approximately 370,000 inhabitants in 2001. The area includes the municipalities Botkyrka, Huddinge, Nykvarn, Salem and Södertälje, and the sub-municipalities Hägersten, Liljeholmen, Skärholmen and Älvsjö in Stockholm municipality. All 4,188 children attending 8th grade of municipal schools in 2000 or 9th grade in 2001 were identified from the school registers of the municipalities and invited to participate in the study. Of all invited adolescents, 10.5% declined to participate and 4.8% did not participate due to sick leave or other absence from school at time for data collection. Totally, 3,548 (84.7%) adolescents participated in the study.

Study population

Paper I

Paper I compared the BMI-distribution of children born 1973-75, as presented in the paper *He Q, Albertsson-Wikland K, Karlberg J. Population-based body mass index reference values from Göteborg, Sweden: birth to 18 years of age. Acta Paediatrica 2000; 89:582-592,* with the distribution of the children in the COMPASS study, born 1985-87. The older cohort consisted of 3,650 children born at term, i.e. between 37 and 42 gestational weeks, from the greater Gothenburg area. Of the 5,111 eligible children, 623 declined participation, 529 children were lacking birth data, of whom 242 were born in other countries, 218 were excluded due to multiple births, pre-term or post-term birth and, lastly, 91 children were excluded due to chronic diseases or major maternal health problems during pregnancy. Children with allergic diseases such as asthma were included. After the exclusions described above, the cohort born 1973-75 comprised 3,650 children.[171]

The inclusion criteria for the 1973-75 cohort were strictly applied to the 1985-87 cohort. We excluded 612 children lacking birth data, of whom 447 were not born in Sweden, 213 were excluded due to multiple births, pre-term or post-term birth and 47 children were excluded due to chronic diseases or major maternal health problems during pregnancy. Children with allergic diseases such as asthma were included. Of the remaining 2,676 children, 1.4% were born in 1985, 92.4% in 1986 and 6.2% were born in 1987. In the present study only BMI values measured ± 3 months from the following exact ages were used: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and 15 years. Of the 2,676 children, 85 did not have any BMI value within these ranges and were therefore excluded. The remaining 2,591 children comprised the 1985-87 cohort.

Paper II

Paper II investigated the associations of prenatal and postnatal growth with body size and body composition at age 15 among the adolescents in the COMPASS study. In the analyses we excluded 577 children due to missing data on birth weight, birth length or gestational age and 293 children because they were twins, had a severe disease or handicap that affects growth or because of implausible values (±5 SD) on length or weight at birth or at one year of age. Further, 225 children were excluded due to missing information on the outcome variables, i.e. height, weight, BMI, FFM, FM, %FM and WC, or on mother's educational level in 1990 when the children were, on average, four years old. In total, 2,453 children, 1,198 girls and 1,255 boys, comprised the study population.

THE PITCH STUDY (PAPER III)

The paper investigating associations between parents' and children's physical activity was based on the PITCH study – Parental influences on their children's health. The PITCH dataset was created by a record linkage between several Swedish national registers in the year of 2000. From the database parents born in a Nordic country with children born in Sweden during 1988 and 1989, all alive and living in Sweden in 1999, were selected. Parents were selected according to a baseline BMI in order to create groups of both normal weight and overweight parents. Baseline BMI was retrieved from the Military Service Conscription Register at age 18 for the fathers, and from the Medical Birth Register (MBR) for the mothers, as the pre-pregnant BMI. This implies a higher mean BMI among the parents in the present study than the average for the adult Swedish population. The aim of this sampling procedure was to obtain enough children with overweight and obese parents to be able to explore associations between child and parental health related factors in families with one overweight/obese parent as well as in families with two normal weight parents. In total, 5,460 families, with equal numbers of boys and girls, were invited to participate in the study. A total of 1,931 (35%) families responded to at least one of the three questionnaires administered.

Study population

To be included in the analyses of paper III, the child, mother and father had to have complete information on the study variables, i.e. physical activity, self esteem, BMI and potential confounders. Nine families were excluded due to chronic diseases that might have affected their ability to be physically active. Totally 1,124 children, 571 girls and 553 boys, and their parents comprised the study population.

THE SWEDISH YOUNG MALE TWINS STUDY (PAPER IV)

Paper IV, examining the impact of genetic and environmental factors on physical activity, was based on the Swedish Young Male Twins Study, which started in 1998.[172] The Swedish Young Male Twins Study comprises all 3,566 male twins (1,783 pairs) born 1973-1979 listed in the MBR, to which more than 99% of all births in Sweden are reported, and residing in Sweden in 1997.

Study population

The 3,566 twins were asked to answer a mailed questionnaire in 1998. Of these, 2,810 (79%) returned the questionnaire and 2,726 twins had complete information on physical activity. 2,064 twins were classified as either MZ or DZ and part of a complete pair. Ten pairs were excluded due to severe handicaps or diseases and a total of 2,044 twins were included in the analyses. In 2002, 3,484 twins were followed up with a second questionnaire. Of these, 2,169 (62%) responded and 2,078 had information on at least one physical activity dimension (please see below). 1,490 twins were classified as MZ or DZ and part of a complete pair, of whom 248 twins (124 pairs) gave discordant answers on contact frequency and were therefore excluded. Four pairs were excluded due to severe handicaps or diseases. A total of 1,234 twins were included in the analyses of the survey 2002.

SOURCES OF INFORMATION

Weight and body mass index during childhood (Paper I and II)

Data to explore the changes in the BMI-distributions of Swedish children during a 12 year period (paper I) was collected from child health center records and school health records. Length or height and weight during the first years of life are routinely measured and kept in records at child health centers and from school age in schools. Height and weight at age 15 in the COMPASS study, from which BMI at 15 was calculated, were measured by trained nurses according to a study protocol.

To explore the associations of prenatal and postnatal growth with body composition in adolescence (paper II), data on birth weight, birth length and gestational age was obtained by record linkage to the MBR. Birth weight and birth length were converted to sex- and gestational age-specific z-scores using information from MBR on all births during the years 1985-87 in Sweden as external reference. Information on height and weight during childhood was collected from the child health centre records. Height and weight growth curves were fitted for each child and weight and length at one year of age were derived from these growth curves. Weight and length at one year of age were then converted to internally referenced z-scores for boys and girls separately. Birth weight z-score, weight at one year z-score and change in weight z-score during the first year of life were used as predictor variables in paper II.

Body size and body composition in adolescence (Paper II)

The outcome variables in paper II, height, weight, BMI, FFM, FM, %FM and WC, were measured by trained nurses according to a study protocol. Height was measured twice to the nearest 0.5 cm and weight to the nearest 100 g. The averages of the two respective measurements were used in the analyses. BMI was then calculated as weight in kg/height in m^2. The school measurement devices were used after calibration with the project's equipment. If weight systematically differed with more than 0.2 kg and height with more than 0.5 cm the project's equipment was used. FFM and FM were derived from resistance measured with bioelectric impedance analysis (Quantum II, RJL Systems, Clinton Township, MI, USA). This device measures resistance and reactance with the study subjects lying down and a standard conduction current through electrodes placed on the right hand and right foot. FFM was calculated using the cross-validated equation recommended by Houtkooper et al.[159] FM was calculated by subtracting FFM from weight. WC was measured twice to the nearest 1 mm at the minimum circumference between the iliac crest and the rib cage and the average of the two measurements was used.

Physical activity (Paper III and IV)

Information on physical activity was assessed with questionnaires in both PITCH and the Swedish Young Male Twins Study. In the twin study (paper IV), the following two questions were used both 1998 and 2002: “How physically active have you been in your daily work, studies or occupation during the last 12 months?” and “How physically active have you been in your leisure time during the last 12 months?” The response alternatives were 1) sedentary work/leisure time, 2) light activity (not sweating), 3) moderate activity (sweating), and 4) vigorous activity (sweating and breathing hard).

A modified version of the widely used Baecke questionnaire was included in the twin questionnaire 2002.[173,174] The Baecke questionnaire has three dimensions and a summary scale: 1) occupational physical activity, 2) leisure time physical activity excluding sport, 3) sport during leisure time, and 4) total physical activity. The questionnaire has been validated against the DLW method and the correlation between the summary scale total physical activity and physical activity level according to the DLW was 0.69 (standard error =0.13).[175] The Baecke questionnaire was also used among the adults in PITCH (paper III). Paper III focused on possible influences of parents’ sport activities on children’s participation in sport and vigorous activities and therefore only the dimension “sport during leisure time” was used. Parental physical activity was also assessed by the question: “Do you usually participate in sport or exercise activities during leisure time?” with the response alternatives “yes” or “no”.

In PITCH, the children’s sport participation was assessed with the question “Do you usually participate in sport or exercise activities during leisure time?” with the response alternatives “yes” or “no”. Their vigorous physical activity was assessed with the question “How many days during the past week have you participated in vigorous activity for at least 20 minutes that made you out of breath and sweating?”. The response alternatives were 1) none, 2) one day, 3) two days, 4) three days, 5) four days, 6) five days, 7) six days, and 8) every day.

Self-esteem and athletic competence (Paper III)

Paper III also investigated whether the children’s self esteem and athletic competence mediated associations between parents’ and children’s participation in sport and vigorous activities. The children’s self-esteem and athletic competence were assessed with Harter’s Self-Perception Profile for Adolescents, which has been revised and validated in Norway.[144,176] The Norwegian version consists of seven domains, each measured with five statements with four options to decide on; 1) “Describes me very poorly”, 2) “Describes me quite poorly”, 3) “Describes me quite well”, and 4) “Describes me very well”. Two domains, global self worth and athletic competence, were used in paper III. Global self worth measures how much someone likes him- or herself as a person and athletic competence measures, as previously described, children's perceptions of their own ability in sport and outdoor activities.[144] The two variables were categorized in tertiles for boys and girls separately when used as dependent variables, while the original variables were used when introduced in the models as a covariate.

STATISTICAL ANALYSES

Paper I

The BMI values at the 5th, 10th, 25th, 50th, 75th, 90th and 95th percentiles at the following exact ages (± 3 months) were compared between the cohorts born 1973-75 and 1985-87: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and 15 years.

In comparison of BMI distributions between two cohorts from different geographical areas and decades, a crucial issue is whether the cohorts diverge in a way that could explain observed differences. To shed light on potential socioeconomic differences between the Gothenburg (older) and the Stockholm (younger) study cohorts we conducted supplementary analyses on a separate dataset from Statistics Sweden, covering both study areas and containing information about the households (parents) of all children born in 1974 in the municipality of Gothenburg and in 1983 in the study area of Stockholm (register data from 1986 not available). The Stockholm and Gothenburg study areas were compared with respect to highest parental education level and household socioeconomic index. The analyses of parental education level were carried out using the Population and Housing Census of 1990 and the Longitudinal Database on Education, Income and Employment from 1999. When analyzing household socioeconomic index, the Population and Housing Censuses of 1980 and 1990 were used. The distributions were compared with the Wilcoxon's rank-sum test.

Paper II

The height and weight growth curves, from which length and weight at one year of age were derived, were estimated with a non-parametric regression method, so called Kernel estimation,[177] using the *lokern* package in the R software (http://www.r-project.org). Pearson correlation coefficients between predictor and outcome variables were calculated. Associations between birth weight and postnatal growth and the measures of body size/composition were assessed with multiple linear regression analyses according to a strategy proposed by Lucas et al.[178] The linear regression model

$$Y=a+a_1*W_1+a_2*W_2 \quad (1)$$

can be rewritten as

$$Y=a+a_2*(W_2-W_1)+(a_1+a_2)*W_1 \quad (2)$$

where W_1 is birth weight z-score, W_2 is weight at one year z-score and (W_2-W_1) represents change in weight z-score between the two measurements. Equation (2) allows us to interpret the coefficient a_2 as an estimate of the effect of growth during the first year of life, adjusted for birth weight (with the coefficient for birth weight equal to the sum of the early and late weight coefficients).[178,179] According to equation (1), the coefficient a_1 is interpreted as birth weight z-score adjusted for weight at one year z-score.

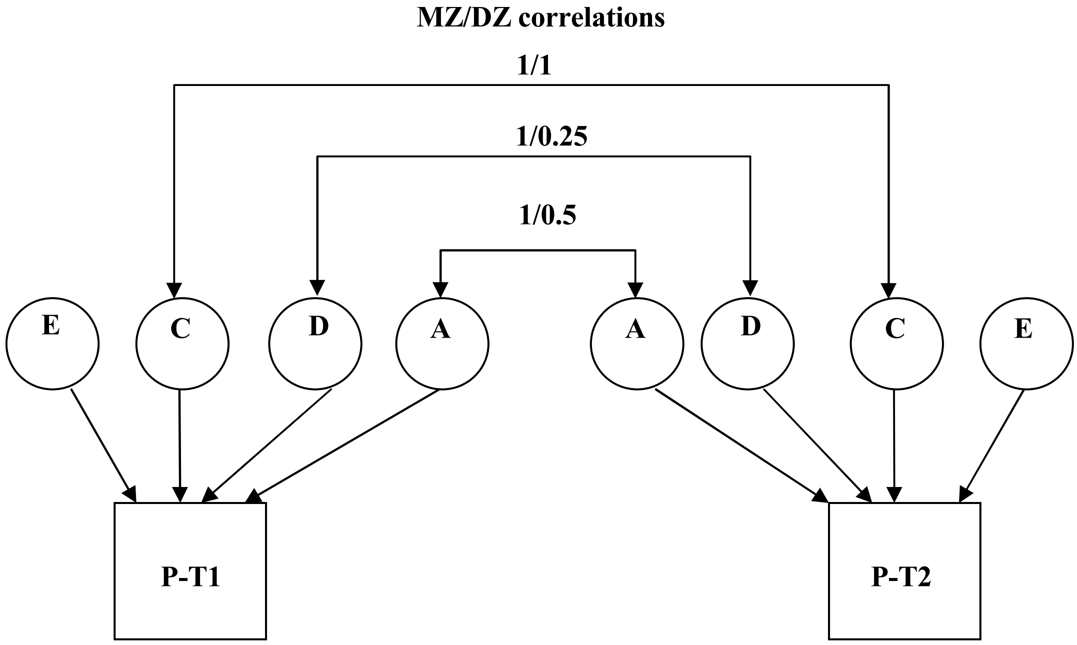
Paper III

To estimate associations between parents' and children's sport participation and vigorous physical activity, prevalence ORs were calculated with logistic regression modeling. To examine whether global self worth or athletic competence were mediating the effects, the following criteria, established by Baron and Kenny[180] were evaluated: 1) We investigated whether the independent variables (parents' sports participation and "sport during leisure time" according to the Baecke questionnaire) were affecting the proposed mediators (athletic competence and global self worth); 2) We continued by studying whether the dependent variables (children's sport participation and vigorous physical activity) were affected by the independent variables; and 3) Finally, we investigated whether the proposed mediators did attenuate the associations between the independent and the dependent variables.

Paper IV

In the twin study, structural equation modeling (SEM) was used in univariate heritability analyses of the different dimensions of physical activity. The total phenotypic variance can be decomposed into the four latent (unmeasured) variance components: additive genetic effects (A), non-additive (dominance) genetic effects (D), environmental effects *shared* by individuals (C) and environmental effects *not shared* by individuals (E), as illustrated in figure 2. Heritability in the broad sense is defined as the proportion of the total phenotypic variation that is due to the genetic components A and/or D.[181] Under this genetic model, SEM can be used to estimate the variance components from which heritability estimates can be derived.

To investigate the EEA, the absolute within-pair score differences on the Baecke questionnaire were assessed with a linear regression model, adjusted for zygozity, and comparisons were made between groups with frequent and infrequent contact between the twin brothers.



P=phenotype, T1=twin 1, T2=twin 2
A=additive genetic effects, D=dominance genetic effects
C=environmental effects shared by the twins, E=environmental effects not shared by the twins

Figure 2. Path diagram for univariate analyses.

4 RESULTS

CHANGES IN BMI-DISTRIBUTIONS OF SWEDISH CHILDREN (PAPER I)

Paper I compared BMI-distributions at ages 2-15 between two Swedish population-based cohorts born 1973-75 and 1985-87. The comparisons showed no differences in early childhood but there were discernible differences from 5-6 years of age. From age 6, girls born 1985-87 and belonging to the upper parts of the BMI-distribution, e.g. those above the 90th or 95th BMI percentiles, had much higher BMI values compared to their counterparts born 12 years earlier (figure 3), i.e. the distributions were more skewed to the right in the younger cohort. The patterns were similar among boys. The differences between the distributions appeared above the 25th percentile and became increasingly pronounced in the upper parts of the BMI-distributions (figure 4). Further, the skewness increased with age. At age 15 the median differences were 0.5 kg/m^2 for boys and 0.4 kg/m^2 for girls and the differences for P95 were 2.4 kg/m^2 and 2.3 kg/m^2, respectively.

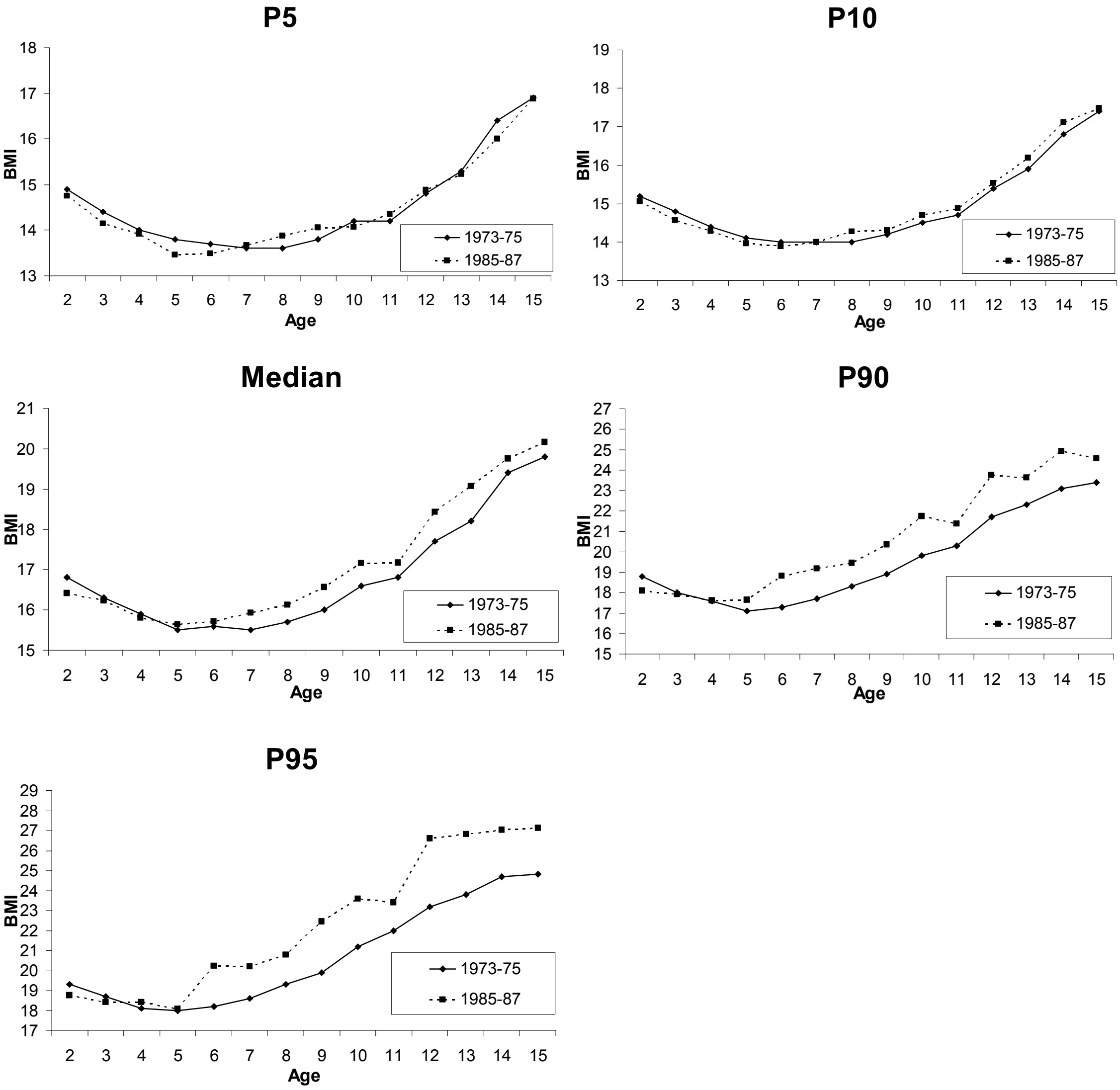


Figure 3. Comparisons of BMI-values for P5, P10, the median, P90 and P95 of the BMI-distributions of girls born 1973-75 and 1985-87.

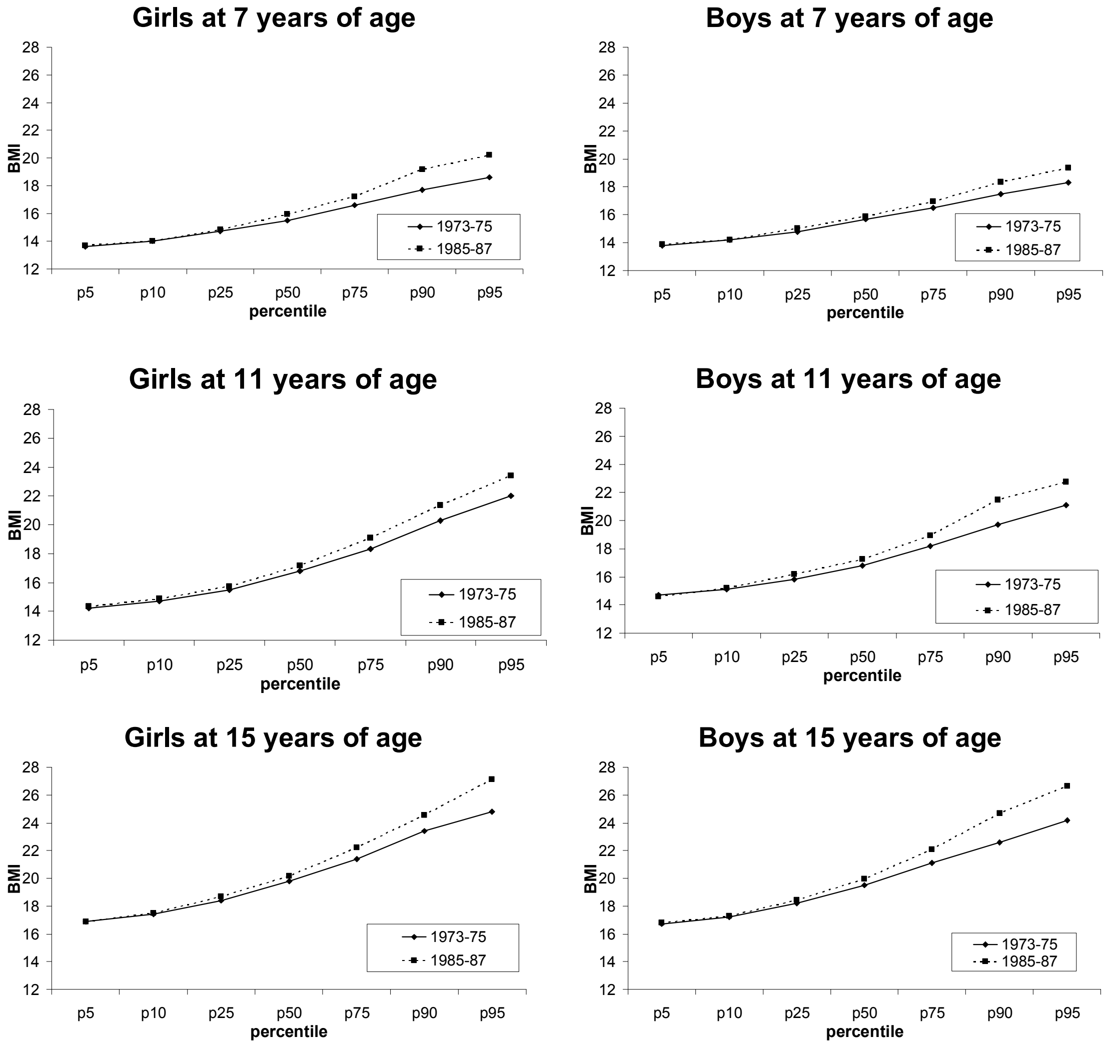


Figure 4. Comparisons of the BMI-distributions of children born 1973-75 and 1985-87 at 7, 11 and 15 years of age.

EARLY GROWTH AND BODY COMPOSITION IN ADOLESCENCE (PAPER II)

Paper II showed that both prenatal growth, as measured with birth weight z-score, and postnatal growth during first year of life, measured as change in weight z-score, were positively associated with body size and body composition at age 15. The only exception was %FM among girls, which was not related to prenatal growth. The adjusted effects are presented in table 1. For one SD increase in birth weight, BMI increased with 0.73 and 0.33 units among boys and girls respectively. The corresponding figures for FFM were 1.66 kg (boys) and 1.05 kg (girls). Postnatal growth was more strongly associated with body composition in adolescence. One unit increase in weight z-score during first year of life was associated with 1.11 and 1.32 units increase in BMI among boys and girls respectively. For FFM the corresponding figures were 2.30 kg (boys) and 1.64 kg (girls). There was no indication of any effect modification of birth weight on the associations between postnatal weight gain and body composition in adolescence, when modeled as an interaction between the two variables in the regression model.

Table 1. Effects of prenatal and postnatal growth on body composition in adolescence. Mean (95% CI).

		Prenatal weight gain[1]	Postnatal weight gain[2]
Boys	BMI (kg/m^2)	0.73 (0.47; 0.98)	1.11 (0.87; 1.35)
	FFM (kg)	1.66 (1.08; 2.25)	2.30 (1.76; 2.83)
	FM (kg)	0.75 (0.27; 1.23)	1.18 (0.71; 1.65)
	FM (%)	0.42 (-0.10; 0.93)	0.80 (0.29; 1.30)
	WC (cm)	1.32 (0.67; 1.96)	1.82 (1.20; 2.44)
Girls	BMI (kg/m^2)	0.33 (0.07; 0.59)	1.32 (1.06; 1.59)
	FFM (kg)	1.05 (0.63; 1.47)	1.64 (1.23; 2.06)
	FM (kg)	0.38 (-0.07; 0.84)	1.87 (1.41; 2.33)
	FM (%)	-0.10 (-0.53; 0.33)	1.49 (1.04; 1.93)
	WC (cm)	0.85 (0.26; 1.44)	2.59 (2.00; 3.18)

[1] Per 1 SD increase in birth weight

[2] Per 1 unit increase in weight z-score during first year of life

Figure 5 further illustrates the associations of prenatal and postnatal growth and BMI, FFM and FM in adolescence. Separating the increase in BMI (weight/height^2) into FFM/height^2 and FM/height^2, show that the increase in BMI associated with prenatal weight gain was mainly due to increase in FFM, especially among girls. On the contrary, increase in BMI associated with postnatal growth was due to increase in both FM and FFM. Among girls, the relative effect of postnatal growth on FM vs. FFM was larger compared with the effect of prenatal growth. This was not the case among boys.

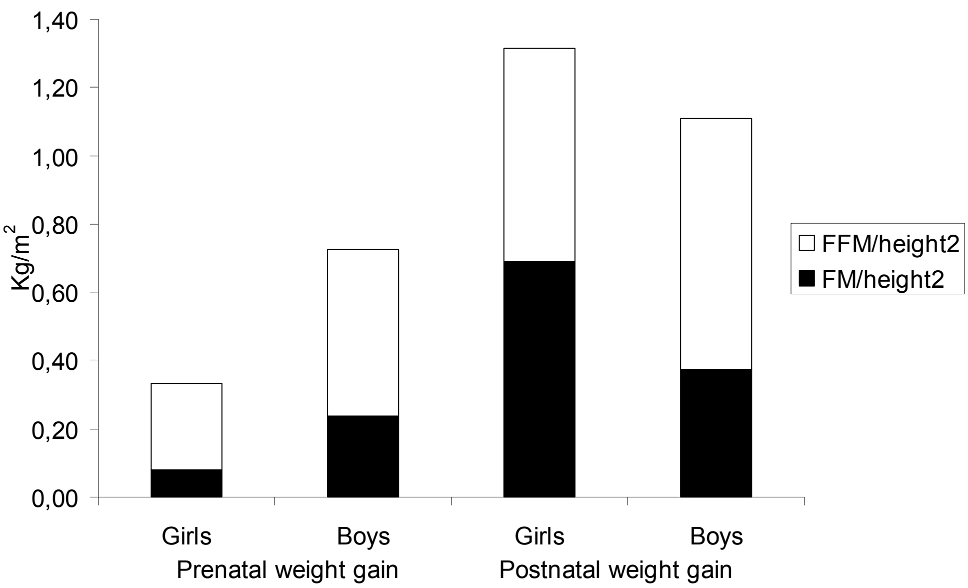


Figure 5. The changes in BMI (weight/height^2) associated with pre- and postnatal growth separated into changes in FFM/height^2 and FM/height^2.

FAMILY ASSOCIATIONS IN PHYSICAL ACTIVITY (PAPER III)

Paper III, examining relations between parents' and 12 year-old children's physical activity, found that both mothers' and fathers' participation in sport activities and level of sport during leisure time were strongly associated with their children's participation in sport and vigorous activities. Further, compared with the fathers' activity, mothers' participation in sport seemed to be more strongly associated with girls' physical activity. The opposite was the case for boys. In addition, there seemed to be a combined effect of mothers' and fathers' participation in sport activities in relation to boys' participation in sport activities. Figure 6 shows the OR for boys and girls sport participation when they have none, one or two active parents. The increase in boys OR from 2.5 (95% CI, 1.4; 4.5) when having an active mother only, and 3.2 (1.5; 6.6) when having an active father only, to 8.8 (4.3; 18.0) when having two active parents suggests a synergistic effect of 4.1. Similar interaction was not observed among girls.

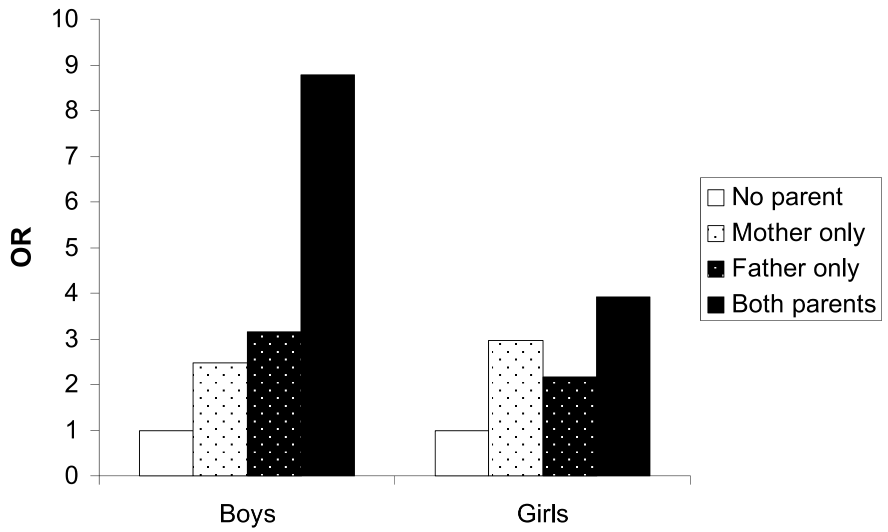


Figure 6. ORs for children to participate in sport activities related to parents' sport participation.

Paper III also investigated whether the children's global self worth and athletic competence mediated the associations between parents' and children's physical activity. Global self worth was not mediating the associations. Athletic competence seemed to have a mediating effect on boys' participation in sport activities and vigorous physical activity when both parents were participating in sports or the father was high active according to the sport during leisure time dimension of the Baecke questionnaire.

GENETIC FACTORS IN PHYSICAL ACTIVITY (PAPER IV)

Paper IV examined the contribution of genetic and environmental factors to physical activity. The within-pair correlations for the different dimensions of physical activity were about twice as high for MZ compared with DZ twins, indicating presence of genetic effects.

The best fitting SEM model for all dimensions of physical activity was the AE-model, which suggests that physical activity is influenced by additive genetic (A) and non-shared environmental factors (E). In 1998, the heritability estimates for occupational physical activity and leisure time physical activity including sport were 0.60 (95% CI, 0.53; 0.65) and 0.65 (0.59; 0.70), respectively. The corresponding heritability estimates for 2002 were somewhat lower, 0.54 (0.44; 0.62) and 0.55 (0.46; 0.63), respectively. The heritability analyses of the different dimensions of the Baecke questionnaire are presented in table 2. The highest heritability estimate was obtained for occupational physical activity and the lowest for leisure time physical activity excluding sport.

Table 2. Heritability (a^2) of the physical activity (PA) dimensions measured by the Baecke questionnaire.

Dimension of physical activity	MZ pairs N	DZ pairs N	a^2 (95% CI)	e^2 (95% CI)
Total PA	305	170	0.49 (0.40-0.56)	0.51 (0.44-0.60)
Occupational PA	323	195	0.57 (0.50-0.64)	0.43 (0.36-0.50)
Leisure time PA excluding sport	357	227	0.40 (0.31-0.48)	0.60 (0.52-0.69)
Sport during leisure time	356	222	0.56 (0.49-0.62)	0.44 (0.38-0.51)

a^2 Additive genetic factors

e^2 Non-shared environmental factors

To examine whether the EEA might be invalid for physical activity in this twin population, the means of the absolute within-pair score differences on the Baecke questionnaire, adjusted for zygosity, were compared between twins with frequent and infrequent contact.[182] The differences were -0.024 for occupational physical activity (P=0.47), 0.034 for leisure time physical activity excluding sport (P=0.13), 0.008 for sport during leisure time (P=0.84), and 0.012 for total physical activity (P=0.87). Results from the same analyses performed on MZ and DZ twins separately did not show any significant differences. Nor was there a significant interaction between contact frequency and zygosity for any physical activity dimension. Thus, these results do not indicate a violation of the EEA, as measured with contact frequency between the twins.

5 DISCUSSION

CHANGES IN BMI-DISTRIBUTIONS OF SWEDISH CHILDREN

In accordance with paper I, several previous studies have reported major changes over time in the upper parts of the BMI-distribution.[69,74-76] This indicates that individuals in the upper parts of BMI-distributions have been affected more by the environmental changes in society during the last decades than individuals in the lower parts of the distributions. Segments of the population may thus be more genetically susceptible to environmental changes than others, resulting in increased skewness to the right of BMI-distributions, which also has been suggested in previous studies.[183] Our observation that the changes in the shape of the BMI-distribution were only discernable from 5-6 years of age neither confirms nor rules out genetic effects. Obesity promoting genes may be incompletely expressed and/or gene - environment interactions may be weak below these ages, as indicated by a study that found no genetic effects on physical activity among 4-10 year old children.[119] Further, environmental changes in society may not have affected young children to the same extent as older children. The energy intake of children above 5-6 years of age may have increased more over time than among children below these ages. This suggestion is supported by recent studies showing that time spent watching television and meals consumed in front of the TV increase with age during childhood.[184,185] Previous studies have also shown that portion size has increased during the last decades for all age groups except for children up to 5 years of age.[186,187]

As mentioned above, Swedish studies on trends in physical activity and sport participation among adolescents have shown that a larger proportion young people were engaged in leisure time physical activities in the 1990's and 2000's compared with the 1960's and 1970's, indicating that EE due to leisure time physical activity has not decreased.[83,84] We are, however, not aware of any reliable information on changes over time in total EE that can be generalized to Swedish children. Therefore, no conclusions can be drawn about the impact of possible changes in physical activity on the observed differences in shape and location of the BMI-distributions.

EARLY GROWTH AND BODY COMPOSITION IN ADOLESCENCE

The strong positive effect of increased weight gain during first year of life on FFM among both boys and girls, is in agreement with previous studies.[110-112] FM, %FM and WC were also positively associated with increased postnatal weight gain, in accordance with another study of Swedish adolescents.[112] Others have, however, failed to show such a relation.[110] Several studies have reported positive associations of increased weight gain in early childhood with overweight and obesity later in life.[10,188,189] However, most previous studies have used definitions of overweight and obesity based on BMI and consequently lacked potential to disentangle the effects of increased weight gain in early childhood on FFM and FM in adolescence or later life. Our results showing 1.11 (boys) and 1.32 (girls) units increase in BMI per unit increase in weight z-score during the first year of life are in agreement with previous findings.[10,188,189]

Prenatal growth, as measured with birth weight z-score, was also positively associated with BMI and FFM later in life, in agreement with previous research.[101-103,190] However, our finding of positive associations between birth weight z-score and FM, although not significant among girls, is in contrast to many previous studies,[102-106] but in agreement with a large study that assessed body composition, including FM, with DXA on children 9-10 years of age.[190]

The effect of increased weight gain during the first year of life was stronger on all measures of body size and composition than the effect of birth weight, both among boys and girls. Prenatal weight gain seemed to have greater effect on boys than girls, whereas the opposite was the case for postnatal weight gain. The larger effect of postnatal weight gain among girls was mainly due to larger increase in FM, which makes sense as girls accumulate more FM during puberty than boys.[44] As mentioned above, it has been suggested that intrauterine growth restricted children compensate with rapid weight gain in infancy, so called “catch-up growth” and that these children have an increased risk of obesity and chronic disease in adulthood.[99,113] In contrast to these previous studies, but in accordance with others,[103,188,189] there was no effect modification of birth weight on postnatal weight gain in relation to any of the outcome measures. Thus, there was no effect of “catch-up growth” on body size or composition. However, different definitions of “catch-up-growth” have been used in other studies.

The strong positive associations of both pre- and postnatal growth with WC at age 15 is in accordance with a previous study of adolescents.[112] The positive association between prenatal growth and WC in adolescence seems contradictory to the inverse association that has repeatedly been reported between birth weight and abdominal obesity, type II diabetes and cardiovascular disease.[98,101] We have no convincing explanation, but speculate that WC in population samples measured in adolescence may not be as good a measure of central obesity as in adulthood.

FAMILY ASSOCIATIONS IN PHYSICAL ACTIVITY

Consistent with previous research, paper III showed associations between parents’ and children’s physical activity.[136,138,191,192] The associations found were, however, much stronger than in most of these earlier studies. This may partly be explained by the fact that we studied associations between parents’ and children’s participation in sport and vigorous activities. Previous family and twin studies have found greater association within families for activities at the upper and lower ends of the physical activity distribution, i.e. sedentary and vigorous activities, than for moderate physical activity.[125,126,136] There are, however, studies that have not found any associations between parents’ and children’s physical activity.[140] Our results show that mothers’ physical activity had a stronger influence on, or at least association with, girls’ participation in sport activities than fathers’ physical activity, whereas fathers’ physical activity influenced boys’ sport participation to a greater extent. The literature is inconsistent on this point.[140] Some studies have not found any differences between the parents’ influence on their children’s physical activity,[192] while others have reported greater impact by mother’s physical activity[138] or of father’s physical activity,[191] regardless of the sex of the child. Possible explanations are that parents' impact on their children decline with age and that mothers and fathers influence their sons and daughters differently depending on the children's age. Wagner et al, who also studied 12-year-old children, found stronger associations between mothers' and daughters' sport participation, in accordance with the findings in paper III.[138]

Self-esteem and self-efficacy have, in previous studies, been shown to be associated with physical activity.[42,139,142,143] In paper III, however, there was no relationship between children's global self worth and their physical activity. This is in contrast to a study of factors associated with longitudinal changes in physical activity among adolescent girls, which also used the global self worth scale by Harter.[143] In the same study, athletic competence was found not to be related to physical activity, which also is in disagreement with the present study where children's athletic competence was strongly associated with their participation in sport activities and vigorous physical activity. Further, paper III provides some support for the notion that athletic competence mediates the association between parents' and sons' sport and vigorous activities and that the father's participation in sport activities is of particular importance in this context.

GENETIC FACTORS IN PHYSICAL ACTIVITY

There are considerable inconsistencies in the literature regarding the magnitude of familial resemblance in physical activity.[127,130] Estimates of intra-class correlations and heritability depend on type of family relations and the studied physical activity dimension. Heritability estimates range from none or weak[123] to moderate[126] and even high.[124] Most studies, but not all, have found no shared environmental effects on physical activity.[130]

Paper IV showed moderate to high genetic contributions to physical activity, heritability in the range of 0.40 to 0.65, depending on physical activity dimension. These estimates are in agreement with several other twin studies.[122,127-129] There was no effect of shared environment in the studied physical activity dimensions. Only additive genetic and non-shared environmental factors seem to be of importance for the variation in physical activity in this young adult male population. The same pattern was seen in a Portuguese study of adolescent and young adult twins. In that study a strong genetic effect was found on leisure time physical activity excluding sport (0.68) and sport during leisure time (0.63) among the male participants and no or weak effect of shared environment.[128] These researchers also used the Baecke questionnaire for assessment of physical activity.

A study of 3,344 middle-aged twin pairs from the USA reported heritability estimates in the range of 0.48 to 0.53 for specific intense activities such as running and racquet sports.[126] Further, these authors suggested that genetic factors might have stronger influence on regular participation in specific intense physical activities than on moderate activities such as walking for recreation or exercise. In agreement with these findings, paper IV showed lower heritability estimates for leisure time physical activity excluding sport than for sport during leisure time (0.40 and 0.56, respectively).

The heritability estimate of occupational physical activity was higher in 1998 (0.64) than in 2002 (0.54). Similarly, the heritability estimate of leisure time physical activity including sport was higher in 1998 (0.65) than in 2002 (0.55). The influence of unshared environmental factors on physical activity may thus increase with age when young adult individuals complete their education, marry and settle down. These observations are in line with another population-based twin study, which showed lower heritability for physical activity among Finnish men 30-39 years of age (0.52) than among those 18-29 years of age (0.64).[122] There are also studies that suggest that genetic effects are absent in childhood and start to appear in late adolescence and then increase into early adulthood.[119,134]

METHODOLOGICAL CONSIDERATIONS

Study design

This thesis was based on four different cohorts, including the comparison cohort from Gothenburg, which all are population-based. Paper I and II were based on the COMPASS study and used prospective information on birth data, height and weight routinely collected in registers and health records. The PITCH study (paper III) is cross-sectional, which implies need for caution in drawing conclusions about cause and effect. This is important when interpreting the observed associations between parents' and children's physical activity. We can not rule out the possibility that children's physical activity is affecting parents to be physically active or that high athletic competence may be an effect of being physically active rather than causing a higher level of physical activity.

In paper III, ORs were calculated to estimate the associations between parent's and children's physical activity. In cross-sectional studies, ORs provide a good estimate of the relative risk when the prevalence of the outcome is low. In paper III, however, the prevalence of participation in sport activities among the unexposed children, i.e. the children with inactive parents, was between 68-78%, implying that the ORs are overestimating the relative risk.

The Swedish Young Male Twins Study (paper IV) has a longitudinal design, but was analyzed cross-sectionally by univariate SEM models. Critique has been directed toward the classical twin study design and it has been claimed that results from twin studies can not be generalized to the rest of the population, since twins are different from singletons in several ways. They have lower birth weights, shorter age at gestation, greater risk of pre- and postnatal complications and higher perinatal mortality than singletons. However, research comparing older twins and singletons has not found any differences, suggesting that any dissimilarity is "washed out" in early life.[193]

It has been claimed, however, that the classical twin design is flawed by higher within-pair correlations among MZ than DZ twins in environmental factors influencing some behavioral traits. Under such circumstances the EEA, i.e. that MZ and DZ twins experience equally correlated environments of etiological importance for the trait, might be invalid and the heritability would be overestimated.[170] In paper IV, no differences in physical activity were found between twin pairs with frequent and infrequent contact, suggesting the EEA to be valid. Even so, a violation of the EEA can not be completely ruled out since there might be other environmental factors not captured by contact frequency that make MZ twin pairs more alike. However, when testing the EEA for eating behavior, Klump et al. did not find support for the hypothesis that within-pair resemblance is affected by degree of physical or other similarities[194] and Evans and Martin found evidence that strongly suggests that the classical twin design does not violate the EEA.[193]

Selection

In the COMPASS study the participation rate was 84.7%, which may be considered high. The study populations in paper I and II were, however, much smaller. In paper I there were some differences between the children included in the younger cohort and those not included regarding the mothers' level of education, 31.9% vs. 26.6% were high educated, whereas there were only small differences in BMI. Further, cohorts born 12 years apart in two large metropolitan areas were compared, making it a key question whether the observed differences between the BMI-distributions could be explained by selection bias or socioeconomic cohort differences. To secure comparability, the inclusion criteria applied for the older cohort born in Gothenburg were strictly followed for the younger cohort born in Stockholm. Both cohorts were restricted to children born in Sweden making the question of ethnic differences less relevant. It seems implausible that the observed differences in the BMI-distributions are due to selection mechanisms influencing the cohorts differently.

We had only access to published data on the Gothenburg cohort and were unable to conduct direct analyses of possible socioeconomic cohort differences. However, we attempted to throw light on such potential differences by analyzing a separate dataset from Statistics Sweden, covering both study areas, with respect to parental educational level and household socioeconomic index. A somewhat larger proportion of parents from Gothenburg were low-educated compared to parents from the Stockholm area but only small differences were seen with respect to household socioeconomic index. A strong inverse association between parental educational level and prevalence of obesity among Swedish young men has recently been reported.[195] Therefore, it is likely that the differences between the BMI-distributions of the Stockholm and Gothenburg cohorts would have been more pronounced if socioeconomic differences had been taken into account in the analyses.

The PITCH dataset was designed to obtain enough children with overweight/obese parents, implying a higher BMI among the parents than in the adult Swedish population. Further, there was a large proportion of non-responders making it an important issue whether the responders differ from the non-responders. Comparisons of the 1,124 families included in the analyses with the 4,336 families not included (due to non-participation or missing data on selected variables) regarding parental BMI from the MBR (mothers) and the Military Service Conscription Register (fathers), showed no differences. Nor were there any differences in current BMI between the included parents and those not included due to missing data. However, a larger proportion of the included parents participated in sport activities than of those not included, but there was no difference in physical activity between included and non-included children. Further, high educated parents were over-represented among those who participated in the study compared with the total sample. Since previous studies have shown a positive association between level of physical activity and socioeconomic status,[49] and due to the sampling procedure, caution is needed in generalizing to all Swedish families with a child born 1988-1989.

In the Swedish Young Male Twins Study, the non-participation rate was high in 2002 (38%), but comparisons between twins with complete or partial non-response to the questionnaire and those actually included in the study showed only small differences. The study participants had somewhat higher educational level than non-participants (41.1% vs. 35.1%), but the groups did not differ with respect to mean age in 2002 or BMI at age 18. It thus seems plausible that the non-response only impacted on our results by decreasing statistical power.

Since the Swedish Young Male Twins Study includes only men, it is not possible to draw inferences about genetic contributions to physical activity in women. Previous studies have found smaller genetic influences on sports participation and daily physical activity for women than men and influences of shared family environment among women.[127,128] The mechanisms through which the genetic influences are expressed are unknown, but might be different for men and women.

Potential information bias

Body size

Birth weight, birth length and gestational age were collected from the MBR, to which almost all births in Sweden are registered. Even though the quality of the MBR is considered high,[196] it is inevitable that errors occur in such a large-scale routine data set. To decrease such errors in our results, subjects with implausible values (±5 SD) were excluded. Length/height and weight during childhood were collected from child health centre records and school health records, where measured data are routinely registered. In a recent dissertation, these longitudinal data were judged to be a valid source for epidemiological studies on growth patterns among Swedish children.[197]

Height, weight and body composition at age 15 in the COMPASS study were measured by trained nurses according to a study protocol. The equipment utilized was calibrated before use. Body composition was assessed with BIA, which is a reasonably good method in population studies, but may overestimate FFM in obese adolescents.[159] The prevalence of obesity was only 3.1% in the study population, so even if FFM was overestimated among the obese, it should not have had any major effects on the associations between early growth and body composition.

Physical activity

Physical activity was self-reported in both PITCH and The Swedish Young Male Twins Study. Self-reported physical activity has been shown to overestimate objectively measured physical activity, among both children and adults.[165,166] Among the parents in PITCH and in the twin study, the Baecke questionnaire was used. As previously mentioned, the questionnaire has shown high validity in comparison with the DLW technique.[175] In the study of associations between parents' and children's physical activity, it seems unlikely that any over-reporting of participation in sport activities among parents would be different across levels of children's physical activity and thereby cause differential misclassification. Children's self-reported physical activity has shown very different validity, mainly dependent on age.[164] Older children seem to report their physical activity more accurately than younger ones. The children in the PITCH study were almost 12 years old, and likely to be able to recall their participation in sport and vigorous activities. Over-reporting of physical activity among children could still be an issue, but it seems unlikely that misclassification would differ across levels of parental physical activity. Further, our results are consistent with other research in the field,[136,138,191] even though the literature is inconclusive.[140] All together, it is most likely that any potential misclassification bias is non-differential, which would lead to underestimation of true associations.

The two questions on occupational physical activity and leisure time physical activity including sport used in the twin study correlated strongly with the corresponding dimensions of the Baecke questionnaire in 2002, 0.85 (95% CI, 0.83-0.86) and 0.82 (95% CI, 0.81-0.84) respectively, which suggests that they are reasonably good measures of physical activity.

Confounding

Confounding is a central issue in epidemiological research. Confounding occurs when the effect of the exposure is mixed with the effect of another variable.[1] To qualify as a confounder, a variable has to fulfill three criteria; it must be a risk factor for the outcome, it must be associated with the exposure and it must not be on the causal pathway between the exposure and outcome. Even though we had the possibility to control for several possible confounding factors in both the COMPASS and PITCH study, we can not rule out that residual confounding to some extent have affected the results.

Precision

Another issue affecting interpretation of results is precision. Random error, i.e. the influence of chance, leads to lack of precision and is affected by sample size. A large study has a smaller amount of random error than a study with few study subjects. Precision can also be improved by better study design and methods resulting in more and better information on the study subjects. Information on precision is expressed by confidence intervals around the point estimate. A wide interval indicates low precision and a narrow interval high precision. Confidence intervals are, however, set at an arbitrary level, usually 95%, which also affects the width of the interval.

In paper III, the confidence intervals were quite wide. This indicates low precision due to the relatively small sample size. Even when the null value was not included in the 95% confidence intervals, making the null result unlikely, it is difficult to make firm conclusions about the magnitude of the effect. This is important to consider when interpreting the results.

CONCLUDING REMARKS

Different aspects of body size and physical activity among children and young adults were investigated. Paper I showed that BMI-distributions were more skewed to the right among Swedish children born in the 1980's compared with those born in the 1970's, i.e. the heavy children became heavier. The prevalence of genes increasing susceptibility to obesity is not likely to have changed over such a short time period, indicating environmental changes that possibly interact with genetic factors.

Growth in prenatal life and infancy was positively related to BMI and body composition in adolescence, as shown in paper II. Postnatal growth had stronger effect than prenatal growth on all measures of body composition.

As mentioned previously, physically active children have greater increase in FFM and less accumulation of FM compared with inactive children. As a consequence, two children with the same BMI might have different proportions of FFM and FM. This emphasizes that it is important to separate FFM from FM when studying overweight and obesity, especially among growing children.

Paper III showed strong associations between parents' and children's participation in sport and vigorous physical activity and that children's athletic competence might be a mediating factor. Paper IV showed that genetic factors influence physical activity. The genetic effect seemed to be stronger on sport activities than on other leisure time physical activities. There was no effect of shared environmental factors on any of the physical activity dimensions among the young adult male twins. This may seem contradictory to the strong associations between parents' and children's participation in sport activities. However, it is conceivable that contributions of genetic and shared environmental factors to physical activity are age dependent with weaker genetic effects until late adolescence, as indicated by some previous research.[119,134]

6 SAMMANFATTNING (SUMMARY IN SWEDISH)

Det övergripande syftet med avhandlingsarbetet var att utöka kunskapen om olika aspekter av kroppsstorlek och fysisk aktivitet bland svenska barn, ungdomar och yngre vuxna. Specifika syften var: (i) att undersöka hur BMI-fördelningarna har förändrats under en 12 års period, (ii) att studera vilken betydelse tillväxt under fosterlivet och under det första levnadsåret har för kroppsstorlek och kroppssammansättning vid 15 års ålder, (iii) att studera samband mellan föräldrars och barns fysiska aktivitet, samt (iv) att undersöka vilken betydelse genetiska faktorer har för fysisk aktivitet.

Studien av hur BMI-fördelningarna förändrats utgick ifrån en jämförelse mellan två populationsbaserade material; en kohort med 3650 barn födda 1973-75 och en kohort med 2591 barn födda 1985-87 – COMPASS-studien. Jämförelsen visade på stora skillnader i BMI-fördelningarna från 5-6 års ålder, med högre BMI-värden i den yngre kohorten. Inga skillnader fanns för 2-5-åriga barn. Förändringarna började framträda vid den 25:e percentilen och ökade sedan i de övre delarna av fördelningarna, dvs. de överviktiga barnen blev mer överviktiga under 12 års perioden.

COMPASS-studien användes också för att studera betydelsen av tillväxt under fosterlivet och första levnadsåret för kroppsstorlek och kroppssammansättning vid 15 års ålder. Tillväxten under fosterlivet mättes med köns- och gestationsålders-standardiserad födelsevikt, s.k. z-score, och uppvisade positiva samband med BMI, fett fri kroppsmassa, fettmassa och midjeomfång. För varje enhets ökning i födelsevikt z-score ökade den fettfria massan med 1.66 kg för pojkar och 1.05 kg för flickor. Det förelåg även ett positivt samband mellan tillväxt under fosterlivet och andel fettmassa bland pojkarna, men inte bland flickorna. Tillväxt under det första levnadsåret mättes med förändring i vikt z-score mellan födelsen och ett års ålder och var starkt relaterat till samtliga mått på kroppssammansättning vid 15 års ålder. För varje enhets ökning i vikt z-score under det första levnadsåret hade pojkarna 2.30 kg större fettfri kroppsmassa. Motsvarande värde bland flickorna var 1.64 kg. Tillväxt under det första levnadsåret hade starkare samband med kroppssammansättning än tillväxt under fosterlivet.

Studien av samband mellan föräldrars och barns fysiska aktivitet baserades på PITCH-studien. Studiepopulationen bestod av 1124 12-åringar och deras föräldrar. Föräldrarnas fysiska aktivitet hade starka samband med barnens deltagande i idrottsaktiviteter och hård fysisk aktivitet. Oddskvoten för att barn med två idrottsaktiva föräldrar skulle delta i idrottsaktiviteter var 3.9 (95 % konfidensintervall, 2.2;6.9) (flickor) och 8.8 (4.3;18.0) (pojkar) jämfört med barn till två inaktiva föräldrar.

The Swedish Young Male Twins Study låg till grund för studien av genetiska faktorers betydelse för fysisk aktivitet. Studiepopulationen utgjordes av 2044 manliga tvillingar födda 1973-79. Genetiska faktorer hade måttlig till hög effekt på fysisk aktivitet, med heritabilitetsestimat mellan 0.40 och 0.65 beroende på dimension av fysisk aktivitet. Endast additiva genetiska faktorer och individuella miljöfaktorer hade betydelse för fysisk aktivitet i denna unga manliga population.

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