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GENETIC AND ENVIRONMENTAL EFFECTS ON BODY MASS INDEX DURING ADOLESCENCE: A PROSPECTIVE STUDY AMONG FINNISH TWINS

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Abstract

Objective—To study genetic and environmental factors affecting body mass index (BMI) and BMI phenotypic correlations across adolescence.

Design—Prospective, population-based, twin cohort study.

Subjects and methods—We used twin modeling in 2413 monozygotic and same-sex and opposite-sex dizygotic Finnish twin pairs born in 1983–1987 and assessed by self-report questionnaires at 11–12, 14, and 17 years.

Results—Heritability of BMI was estimated to be 0.58–0.69 among 11–12- and 14-year-old boys and girls, 0.83 among 17-year-old boys and 0.74 among girls. Common environmental effects shared by siblings were 0.15–0.24 among 11–12- and 14-year-old boys and girls but no longer discernible at 17 y. Unique environmental effects were 0.15–0.23. Additive genetic factors explained 90–96% of the BMI phenotypic correlations across adolescence, whereas unique environmental factors explained the rest. Common environment had no effect on BMI phenotypic correlations.

Conclusions—The genetic contribution to BMI is strong during adolescence, and it mainly explains BMI phenotypic correlations across adolescence. Common environmental factors have an effect on BMI during early adolescence, but that effect disappears by late adolescence.

Keywords

body mass index; adolescent; twins; genetics; growth and development; sex specific effects

INTRODUCTION

The etiology of childhood and adolescent obesity is complex. Previous twin studies have estimated the heritability of body mass index (BMI) to be 0.31–0.82 at 1–12 y[1–6] and 0.81–0.90 at 12–19 y[7–10]. However, most of the underlying genes remain unknown: only 7 % of rare, severe, early-onset obesity in children was a result of a monogenic defect[11], and FTO, a

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gene with more common effects on BMI in children and adults, explains only about 1% of the variability of BMI[12]. Few longitudinal twin studies[1,10,13] have explored age-changes of genetic and environmental effects on BMI during childhood and adolescence. Longitudinal twin studies are also needed to explore if factors affecting BMI at separate ages are correlated with each other and to explore relative contributions of genetic and environmental effects on BMI phenotypic correlations across ages, i.e., to find out which factors are responsible for the stability of BMI across ages. Among Dutch children at 3 to 12 y, genetic factors accounted for 57–88%[1] and among Swedish males at 2 to 18 y for 81–95%[13] of BMI phenotypic correlations. The heritability estimates had no systematic age pattern in Dutch children across 3 to 12 y[1] and were quite stable in Swedish boys at 2 to 18 y[13]. Among Australian twins, it was found that the same set of genes accounted for most of the BMI variation at 12, 14, and 16 y, but some new genetic effects emerged at 14 y in girls and at 16 y in both genders; the heritability estimates were stable at 12 to 16 y[10].

BMI in children and adolescents is also affected by environmental factors, such as unhealthy diet, sedentary leisure time, and physical inactivity[14]. Some of these factors are shared by family members while others are uniquely experienced by each individual. Studies in children have often[1–4,6] but not always[5,13] shown that shared family effects are of importance, while cross-sectional studies of adolescents[7–9] or adults[15] show no evidence that these family effects persist beyond childhood. The two longitudinal twin studies conducted in adolescents[10,13] could not substantiate that these effects disappear after childhood, but that might be due to inadequate statistical power in these studies.

Longitudinal studies in large, population-based, adolescent twin samples are required to identify whether shared family effects diminish in importance during adolescence. This is important to identifythe window of opportunity for family-based interventions to prevent weight gain. A large, population-based, prospective cohort of Finnish 11–17-year-old twins[16] gave us this opportunity to study age changes in the contributions of genetic and environmental factors to BMI during adolescence. Because the sample included both same-sex and opposite-sex twin pairs, it was possible also to explore sex differences of these contributions. The longitudinal study setting made it possible to explore the contributions of genetic and environmental factors to BMI phenotypic correlations across adolescence and whether the factors affecting BMI at separate ages are correlated with each other.

METHODS

Participants

FinnTwin12 is a longitudinal study of behavioral development and health habits of Finnish twin children[16]. All twins in the Finnish birth cohorts 1983–1987 were ascertained from the Population Register Center. Twins were assessed by self-report questionnaires at 11–12 y (N=5184, participation rate 92%), 14 y (N=4643, 82% of the original sample), and 17 y (N=4168, 74% of the original sample) of age. Self-report questionnaires were mailed to twin individuals and their parents in the autumn of the year in which their birth cohort reached age 11, and 90% of the responses were received by the end of that year (mean age at response 11.4 y). Twins were sent a follow-up questionnaire in the month of their 14th birthday. Mean age at response was 14.1 years. The last wave (mailed at average age 17.5 y) was completed in 2000–2005. The local ethics committee and the IRB at Indiana University approved the study protocol; written informed consent was obtained from the participating families. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Measures

Zygosity was determined by well-validated items on physical similarity and confusability of appearance at school age. The classification was supplemented by parental response to items developed for zygosity classification of twin children[17]. Assignment of same-sex co-twins, whose zygosity could not be determined definitively from information in twin and parental questionnaires, was supplemented by comparisons of school photographs and additional information obtained from twins' mothers. After exclusion of those whose zygosityremained uncertain (n=340), the final number of participants was 4844, and the final number of complete twin pairs at 11–12 y was 2413 including 796 monozygotic (MZ), 815 dizygotic (DZ), and 802 opposite-sex (OSDZ) twin pairs. BMI (weight/height2) was calculated using self-reported height and weight. Of 4826 participants at 11–12 y, 194 (4%), 134 (3%) of 4350 participants at 14 y, and 75 (2%) of 3929 participants at 17 y had a missing BMI. BMIs below 10 kg/m^2 (3 participants at 17 y) or over 50 kg/m^2 (3 participants at 17 y) were treated as missing, because they were extreme outliers (z-score of log_e-transformed BMI under -5 or over 5). We used log_e-transformed BMI values in the analyses to reduce positive skewness of the BMI distribution. The mean BMI at baseline or at 14 y of those not responding to latter questionnaires did not differ from the mean BMI of those who had responded to them.

Data analysis

MZ twins are genetically identical, while DZ twins share, on average, half of their segregating genes. Thus, if inter-individual phenotypic variance is due to genetic effects, the resemblance within MZ twin pairs will exceed that observed within DZ twin pairs. Genetic effects can be further divided into additive genetic (A), dominant genetic (D), and epistatic effects. If all genetic effects are additive only, meaning that the effect of one allele is added to the effect of another allele at a locus and there is no interaction between alleles, the correlation of genetic effects is 1.0 in MZ twins and 0.5 in DZ twins. A genetic effect due to dominance occurs when the effect of a heterozygote deviates from the mean of homozygote effects. The expected correlation for a dominance genetic effect is 0.25 within DZ twin pairs and results in a lower DZ correlation than when the genetic effect is purely additive. Dominance effects have a correlation of 1.0 in MZ pairs[18]. Epistasis means interaction between alleles at different loci. Epistatic effects are not parameterized in twin models but they are modeled as part of dominance genetic effect if the loci are not linked and as part of additive genetic factors if the loci inherit together due to a close linkage between them.

The resemblance between twins can be due also to effects of common environmental factors shared by co-twins. If twins are reared together, the correlation of the effect of common environment (C) is assumed to be 1.0 in both MZ and DZ twins. Twins also have factors in their environment that they do not share (E, unique environment), the correlation between these effects in MZ and DZ twins is, by definition, zero but E also includes measurement error. A, E, and either C or D can be estimated when employing a design including MZ and DZ twins reared together. These variance components are treated as latent, independent variables which explain the variation of a phenotype, treated as a dependent variable in genetic twin models. Based on the phenotypic variation and co-variation among twins and the known differences in MZ and DZ variance component correlations, it is possible to estimate the magnitude of these variance components using path analysis and structural equation modeling. Classical twin models assume equality of relevant environmental factors for MZ and DZ pairs, random mating and absence of gene-environment interactions[18]. When data from opposite sex pairs are available, then it is possible to test whether the same sets of genes influence variation in BMI in boys and girls. Furthermore, such data permit estimation of the genetic correlation between the effects for males and females[10,19,20].

To study the age changes and sex differences in genetic and environmental effects on BMI, we modeled the variation of BMI at 11–12, 14, and 17 years of age, separately, using univariate twin models. We first tested the basic assumptions of twin modeling at each age by comparison of saturated models to genetic models. Saturated models decompose variation and co-variation of a phenotype as it is: they do not assume equality of means and variances in MZ and DZ twins or in the first and second twin of all pairs. Genetic models assume these and if there is a significant difference in the fit between saturated and genetic models, it means that the basic assumptions of twin modeling mentioned above are not fulfilled. Parameters included in the first genetic model were chosen based on the intra-class correlations. We continued analyses to find the most parsimonious model by testing first whether it is possible to eliminate C or D effects from the full genetic model without decreasing the fit of the model significantly. We then computed a model with parameter estimates (A, C, E) not constrained to be equal for boys and girls and compared this model to a model with equal parameter estimates for both boys and girls to explore if the magnitude of A, C, and E differed between the two sexes. A lower intra-class correlation in OS pairs than in same-sex DZ pairs suggests that some of the genetic effects are not fully shared between males and females i.e. sex-specific genetic effect[10,19,20]. Its existence was tested by estimating additive genetic correlation for OS pairs as a free parameter and testing whether it can be fixed as 0.5, i.e. the same as in SSDZ pairs, without significant worsening of the fit[19]. χ^2-goodness-of-fit statistics and degrees of freedom (d.f.) were used for testing the relative fit of these above depicted hierarchical models.

To study contributions of genetic and environmental factors to BMI phenotypic correlations across ages and to investigate whether genetic and environmental factors affecting BMI at separate ages are correlated with each other, we used a Cholesky decomposition. Cholesky decomposition can be used for multivariate analyses, such as ours, with the BMI assessed at 11–12, 14, and at 17 years of age. This procedure makes no assumptions on the underlying genetic architecture but simply decomposes the variation and covariation in the data into a series of uncorrelated genetic and environmental factors. We chose this approach because our follow-up time was a period of rapid growth and maturation, and therefore it was possible that the genetic architecture of BMI could change across measurements. The structure of the Cholesky decomposition was based on the univariate model fitting results. We adjusted all the models for the participants' exact age at assessment by using age-residualized data. Mx software was used for full information maximum likelihood twin modeling.

RESULTS

The mean BMIs of MZ and DZ boys and girls at 11–12 and 14 y were similar (Table 1). At age 17 years, the mean BMI of DZ boys was higher than the mean BMI of MZ boys (DZ twins 21.9 kg/m^2; MZ twins 21.5 kg/m^2, p=0.007) as was the case among girls (DZ twins 21.1 kg/m^2; MZ twins 20.7 kg/m^2, p=0.007). The standard deviation of BMI increased with age from 2.6 to 3.0 among boys and from 2.6 to 2.7 among girls but when using $\log_e$-transformed values, there was a slight decrease in the standard deviation (1.4–1.3 among boys; 1.4–1.2 among girls).

Intra-class correlations of BMI were higher among MZ than DZ twins (Table 2). Because DZ correlations for BMI were greater than half of the MZ correlations, except among boys at 17 y, the ACE model containing additive genetic (A), common (C) and unique (E) environmental effects was taken as the starting point of the genetic modeling. A lower intra-class correlation in OS pairs than in same-sex DZ pairs indicated a sex-specific genetic effect.

The model fitting results are presented in Table 3. The fit of the models did not worsen when saturated models were compared to ACE models at 11–12 y and at 14 y, and to ACE and ADE models at 17 y, indicating the tenability of the assumptions of the twin modeling. ACE models

were the best fitting models at 11–12 and 14 y; while AE model had the best fit at 17 y. Additive genetic correlation for OS pairs could not be fixed as 0.5 in any age without worsening of the fit, indicating that genetic factors affecting BMI among boys and girls are not all the same. Further, parameter estimates could not be set equal between boys and girls except at age 14 y; for the sake of uniformity and because we had a sample size that made it possible to present parameter estimates separately for both sexes, we present them for boys and girls separately at each age.

Table 4 presents parameter estimates of the univariate models estimating variance structure of BMI at each age, separately. The heritability of BMI was estimated to be 0.58 to 0.69 among 11–12 and 14-year-old boys and girls. It was 0.83 among 17-year-old boys and 0.74 among 17-year-old girls, thus being greater than among younger age groups. The proportion of total variance due to common environmental effects was estimated to be 0.15 to 0.24 among 11–12- and 14-year-old boys and girls. AE models offered the best fit at 17 y, but we present the results from the ACE models in Table 4 to enable comparison of the results to those of 11–12- and 14-year-olds and to confirm that the disappearance of a C component by 17 y was not due to a decreasing statistical power, i.e., a decreased number of participants at 17 y.

The results of the multivariate Cholesky decomposition modeling contributions of genetic and environmental factors to BMI phenotypic correlations are presented in Figures 1 and 2. Based on the model fitting results of the univariate models described in Table 3, we used the ACE model at 11–12 and 14 y and the AE model at 17 y. However, we found that the correlation between common environmental effects affecting BMI at 11–12 and 14 y could be dropped from the model without worsening of the fit ($\Delta\chi^2_2$=0.728, p=0.69), and thus it was removed from the final model.

BMI at age 11–12 correlated strongly with BMI at age 14 among boys (r=0.80) and girls (r=0.74), as did BMI at age 14 with BMI at age 17 (r=0.73 and 0.77, respectively) (Figures 1 and 2). Additive genetic factors explained 92% of the BMI phenotypic correlations between 11–12 and 14 years of age among boys and girls whereas unique environmental factors explained the rest. Of the BMI phenotypic correlations between 14 and 17 years of age, additive genetic factors explained 94% among boys and 90% among girls, while unique environmental factors explained the rest. Of the BMI phenotypic correlations between 11–12 and 17 years of age, additive genetic factors explained 96% among boys and 92% among girls, and unique environmental factors explained the rest. Correlations between additive genetic factors were high: 0.77 to 0.86 among boys (Figure 1) and 0.88 to 0.99 among girls (Figure 2). However, unique environmental factors affecting BMI appeared to change during adolescence as the correlations between them were more modest (0.19 to 0.43 among boys, and 0.25 to 0.40 among girls) (Figures 1 and 2).

DISCUSSION

We studied the contributions of genetic and environmental factors to BMI and BMI phenotypic correlations across adolescence. Our results showed that the common environmental effects (factors shared by family members such as co-twins) present in early adolescence disappeared by late adolescence when the same cohort was followed over time. While additive genetic and common and unique environmental factors affected the variation of BMI both at 11–12 and 14 y, common environmental effects disappeared by age of 17 years and heritability estimates increased. BMI phenotypic correlations across adolescence were mainly explained by additive genetic factors.

Numerous family, adoption and twin studies show that the level of BMI in adults is influenced by additive genetic and unique environmental factors only[15]. Among children and adolescents

the results are more mixed. Most[1–4,6] but not all[5,13] studies have found a significant effect of common environment on BMI among children under 12 y but not among children over 12 y[7–10,13],. While one study found genetic effects due to dominance at 16 y[10], most studies have not documented it among children[1–6,13] or adolescents[7–9,13]. Our study is, to our knowledge, the first follow-up study to demonstrate the disappearance of common environmental effect on BMI in adolescence. Common environmental effects influenced BMI at 11–12 and 14 y, but those effects disappeared by 17 y. Family's socioeconomic status[21], father's parenting style[22], school type[23], and neighborhood characteristics[24] are known to be associated with childhood obesity. These - and probably similar diet and physical activity level among twins of the same family - could account for the common environmental effect on BMI among children and adolescents. In Finland the age of 15–16 y, before the disappearance of common environmental effect at 17 y in our study, heralds the end of compulsory education, allowing the adolescents to get a part-time or full-time job, have more money to spend on their own, spend more time with peers and friends, and even to move away from their parents' home. This can then lead them to make more individualized choices in eating and physical activity patterns, and be less influenced by parental and shared peer effects.

In the previous longitudinal studies conducted in children and adolescents, an ACE model best described BMI phenotypic correlations across ages at 3–12 y in 7755 Dutch twin pairs[1], an ADE model at 12–16 y in 1143 Australian twin pairs[10], and an AE model at 1–18 y in 375 Swedish male twin pairs[13]. The study among Swedish boys may not have had enough statistical power to detect a C or D component because of small number of twin pairs (48–210 pairs according to age)[13]. The Australian study is, to our knowledge, the only one conducted in both genders and in the same age group as ours. The results of the two studies are quite different. In the Australian study[10], an AE model was the best fitting model at 12 and 14 y, but at 16 y, a large dominance genetic effect on BMI was found and in the longitudinal analyses an ADE model offered the best fit. The reasons for the divergent results among Finns and Australians remain unclear. The common environmental effect found among Finns in our study, but not among Australians, could reflect possible differences in family or school environments between these two countries (differences in family meal patterns, school catering, or classroom placement of co-twins). The samples differed too: our Finnish sample was population-based, with a high response rate, thus reflecting the full range of genes and environments present in Finland. The Australian twins were recruited from schools in the greater Brisbane area, through word of mouth and by media appeals[10]. Only 449 pairs participated at baseline and at each follow-up point when compared to 1836 twin pairs in our study. The strength of the Australian study[10] is that weight and height were measured and not self-reported as in our study. MZ correlations in the Australian sample were slightly higher and DZ correlations slightly lower than in our study, and DZ correlations were about half or lower than half of the MZ correlations[10]. The lower genetic diversity of the Finnish population[25] compared to other European populations and presumably to the Australian population could be related to the dominance effect found in Australian but not in Finnish adolescents. However, when genetic and environmental effects on BMI were estimated in young adults aged 20–39 years in eight countries, effects due to dominance or significant differences in the genetic architecture between Finns and Australians were not found[26].

In our study, heritability estimates of BMI increased across the developmental period from 11 to 17 y, as also found previously when studying multiple behavioral phenotypes[27]. The increasing heritability can be attributed to changing gene expression but also gene-environment interaction (GxE), which means that different genotypes respond differently to same environmental factors. In the genetic models used in this study, this effect is modeled as part of genetic effects if the environmental factors are shared within twin pairs and as part of unique environmental factors if not shared[28]. There could be some genes which interact with common environmental factors and whose expression would turn on only at late adolescence, which

could explain the disappearance of C and increasing A component at 17 y. It remains unlikely, however, that disappearance of C would happen only because of this interaction. From the longitudinal model, we can obtain a correlation between genetic effect at 14 y and at 17 y. They are quite high (r=0.82 in boys, r=0.88 in girls), which means that most of the genetic factors influencing BMI at 17 y are actually the same as at 14 y.

Genotype-environment correlation (rGE) means that genetic factors predispose people to certain types of environments. It can be divided to passive, active, and reactive[29]. Passive rGE happens usually in childhood: genes are inherited from parents but parents also provide a large part of the environment for their children. During adolescence the possibilities to choose one's own environment increase and passive rGE gradually turns into active rGE as adolescents have more opportunities to choose environments, exposures and experiences that suit their genotype. Heritability estimates can increase as MZ twins choose more similar environments than DZ twins because of their identical genes and enhance their resemblance to another more than will DZ twins. Genetic factors affecting dietary behaviors[30–34] and physical activity[35,36] and other interests and activities could be these kinds of genetic factors that affect BMI through environmental factors. Active rGE can have an even more pronounced effect nowadays than in the past because most people in affluent countries can freely choose their diet and physical activity level. Twin studies from poorer societies are lacking, but within even affluent societies, the relative contribution of genetic factors to adolescent height and weight could be investigated by socioeconomic gradient given sufficiently large samples.

When using twin modeling, we are not usually able to parameterize epigenetic effects, interaction between genetic and environmental factors, and assortative mating. In a case of positive assortative mating, similar phenotypes mate together. As a result, the genes of offspring are more similar than in the case of random mating, which may increase phenotypic correlations of DZ twins[18] and overestimate the common environmental component[37]. Assortative mating may also conceal the presence of dominant genetic effects and increase the possibility to observe additive genetic effects[18]. Correlations between BMIs of Finnish twins born in 1930–1957 and their spouses were 0.18–0.27[38]. Much of this correlation was, however, explained by social homogamy (choosing a mate based on more similar environmental background), which has no effect on genetic correlations within siblings, rather than phenotypic assortment (choosing a mate based on more similar phenotype)[38]. Further, phenotypic assortment should affect twin correlations in a similar way in all age groups and thus cannot explain the diminishing effect of common environment in this study.

The generalization of the results from twin studies to singleton populations can be uncertain for a phenotype such as BMI. Finnish twins from the FinnTwin16 cohort, especially boys, had lower mean BMI than singletons at 16.5 y[9]. We, however, studied the effects of environmental and genetic factors on BMI using a method based on variation and co-variation of BMI which is not affected by mean values. Family studies have usually yielded heritability estimates lower than twin studies[15,39] but differences in methods can produce these differences[37,39]. Larger heritability estimates in twin studies can also be due to participation bias[40]. There is no perfect method for determining genetic and environmental effects on phenotypes; classic twin modeling remains one of the best, despite its limitations.

We have some limitations in our data. Self-reported weight and height in our study may give rise to self-report bias that tends to lower BMI estimates due to underreporting of weight particularly at the high end of the BMI distribution[41,42]. However, agreement between self-reported and measured values of BMI in different twin samples is good: the correlation between measured and self-reported BMI was 0.83–0.92 among Australian, Finnish, Dutch, and British adult twins[26], 0.97 for height and 0.95 for weight among adult Swedish twins[43]. In twin analysis, self-report bias can lead to decreased heritability estimates and increased E

component, which includes measurement error in addition to unique environmental factors. This is what happened when genetic analyses with measured height were compared to analyses with self-reported height in a same twin sample[39]. Because our heritability estimates were quite large, it is unlikely that they would be greatly deflated because of measurement error. However, it is possible that self-report bias could have affected our results in varying levels at different ages due to different developmental levels. Comparing one's weight response to that of a co-twin could have been more common while still living together at 11–12 and 14 y than at 17 y. This would increase a C component at 11–12 and 14 y. However, we had measured weight and height available from school health records on a random sample of Finnish twins born in 1975–79. At age 11.3 y mean measured BMI of 75 twins was 17.2 kg/m^2 (SD 2.5) which is very close to 17.6 kg/m^2 (SD 2.6) in our data of twins born in 1983–87 at age 11.4 y. Among 80 twins at age 14.1 y mean measured BMI was 19.3 kg/m^2 (SD 3.4) while in our data at age 14.1 y it was 19.4 kg/m^2 (SD 2.7). We also have several strengths in our study cohort including population-based sample of twins of both sexes and of each zygosity, high participation rates, prospective study setting, and standardized age at baseline and at each follow-up point.

In conclusion, common environment has an effect on BMI during early and middle adolescence, but the effect disappears by the end of adolescence. This indicates that, despite strong genetic influence on BMI, family-based interventions hold a promise to control the pediatric obesity epidemic until late adolescence.

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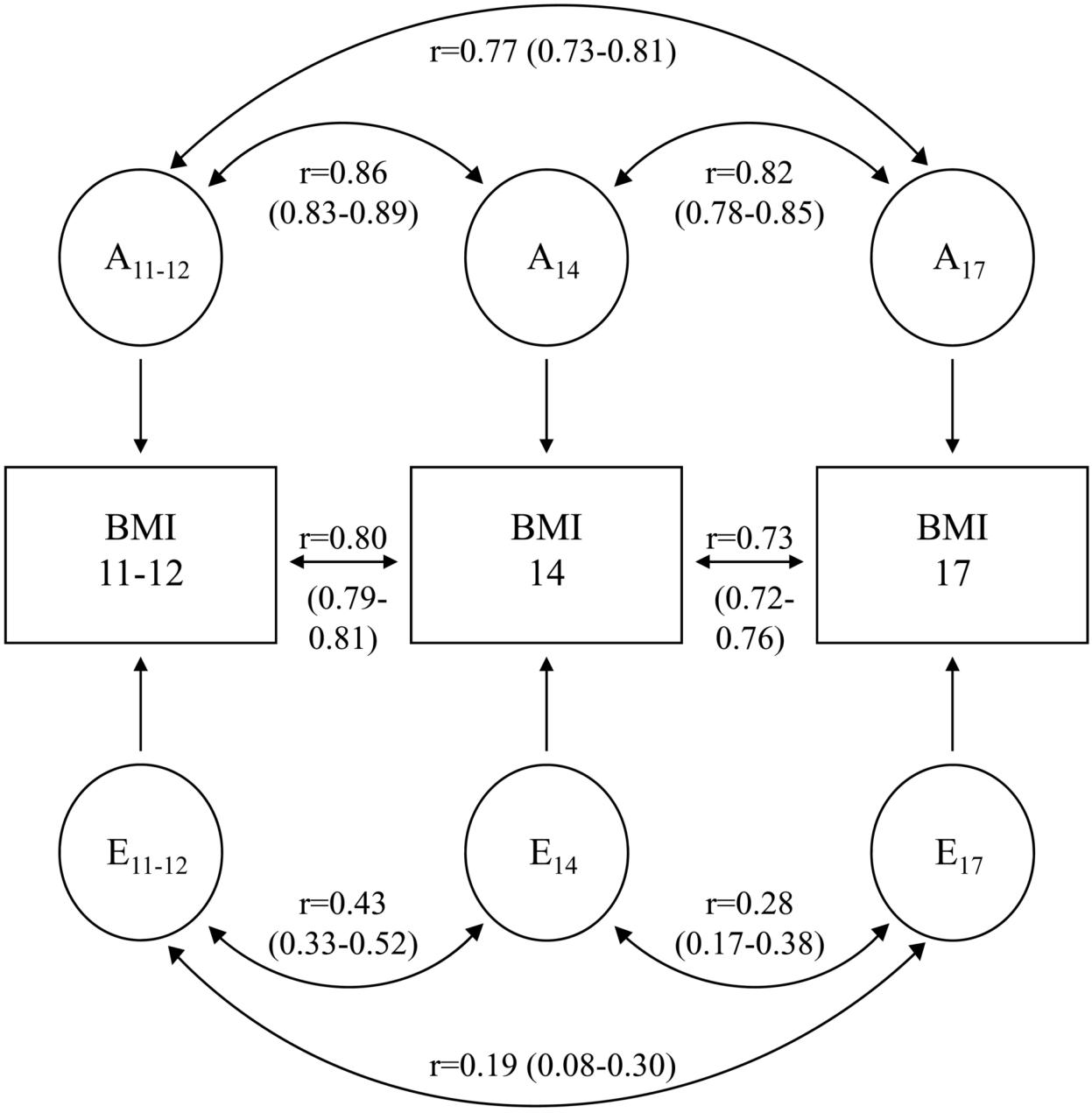

Figure 1. Phenotypic, genetic, and environmental correlations (95% CI) for BMI among boys at ages 11–12, 14, and 17 y

Parameter estimates are based on the trivariate Cholesky decomposition. Additive genetic effects explained 92% of the BMI phenotypic correlation between 11–12 and 14 y, 94% of the BMI phenotypic correlation between 14 and 17, and 96% of the BMI phenotypic correlation between 11–12 and 17 y (r=0.67, 95% CI 0.65–0.70).

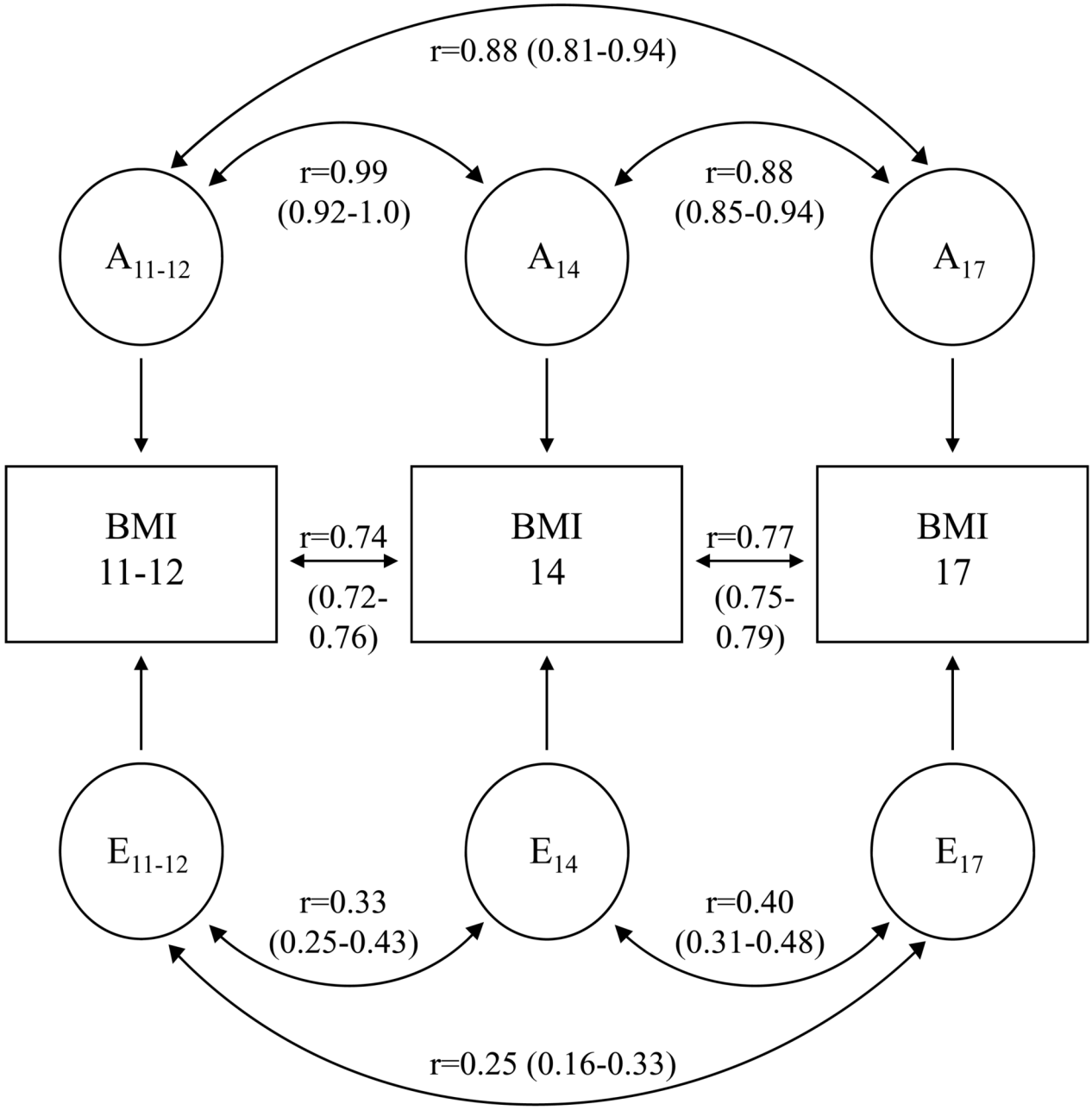

Figure 2. Phenotypic, genetic, and environmental correlations (95% CI) for BMI among girls at ages 11–12, 14, and 17 y

Parameter estimates are based on the trivariate Cholesky decomposition. Additive genetic effects explained 92% of the BMI phenotypic correlation between 11–12 and 14 y, 90% of the BMI phenotypic correlation between 14 and 17, and 92% of the BMI phenotypic correlation between 11–12 and 17 y (r=0.66, 95% CI 0.64–0.69).

Table 1

Means and standard deviations of raw BMI and number of participants.

	Boys			Girls		
	MZ	**DZ**	**MZ and DZ**	**MZ**	**DZ**	**MZ and DZ**
BMI at 11–12 y	17.6 (2.4)	17.8 (2.7)	17.7 (2.6)	17.5 (2.6)	17.6 (2.6)	17.6 (2.6)
n (%)	755 (16)	1618 (35)	2373 (51)	773 (17)	1504 (32)	2277 (49)
BMI at14 y	19.2 (2.6)	19.4 (2.8)	19.3 (2.7)	19.2 (2.6)	19.5 (2.8)	19.4 (2.7)
n (%)	663 (16)	1439 (34)	2102 (50)	726 (17)	1402 (33)	2128 (50)
BMI at 17 y	21.5 (2.7)	21.9 (3.1)	21.8 (3.0)*	20.7 (2.6)	21.1 (2.8)	20.9 (2.7)*
n (%)	589 (15)	1291 (33)	1880 (49)	696 (18)	1280 (33)	1976 (51)

* a significant difference in the mean BMI between boys and girls

Table 2

Intra-class correlations of $\log_e$-transformed BMI with 95% confidence intervals (CI).

	Boys		Girls		Opposite-sex pairs
	MZ	DZ	MZ	DZ	DZ
BMI at 11–12 y: r (95% CI)	0.84 (0.81 to 0.87)	0.50 (0.43 to 0.57)	0.79 (0.75 to 0.82)	0.50 (0.42 to 0.57)	0.41 (0.35 to 0.47)
n of pairs	370	416	377	354	734
BMI at 14 y: r (95% CI)	0.83 (0.79 to 0.86)	0.52 (0.44 to 0.59)	0.81 (0.78 to 0.85)	0.49 (0.40 to 0.57)	0.38 (0.31 to 0.44)
n of pairs	316	355	356	330	666
BMI at 17 y: r (95% CI)	0.80 (0.75 to 0.84)	0.39 (0.29 to 0.48)	0.77 (0.72 to 0.81)	0.39 (0.29 to 0.48)	0.33 (0.25 to 0.40)
n of pairs	282	316	334	309	595

Table 3

Fit of the univariate models for BMI at 11–12, 14, and 17 y.

	BMI 11–12		BMI 14		BMI 17	
	$\Delta\chi^2_2$	p value	$\Delta\chi^2_2$	p value	$\Delta\chi^2_2$	p value
saturated model	-	-	-	-	-	-
- ACE model	20.7	0.19	22.1	0.14	24.6	0.08
- AE model	11.3	0.004	12.3	0.002	0.069	0.97
- no sex-specific genetic effects	55.1	<0.001	4.9	0.028	-	-
- parameter estimates same for both sexes	13.2	0.004	2.3	0.51	-	-
- ADE model	-	-	-	-	24.1	0.06
- AE model	-	-	-	-	0.55	0.91
- no sex-specific genetic effects	-	-	-	-	6.8	0.009
- parameter estimates same for both sexes	-	-	-	-	7.1	0.028

Table 4

Genetic and environmental variance component estimates and 95% confidence intervals for $\log_e$-transformed BMI at ages 11–12, 14 and 17 y under the best fitting univariate models.

	Boys			Girls		
	additive genetic effect	**common environmental effect**	**unique environmental effect**	**additive genetic effect**	**common environmental effect**	**unique environmental effect**
Standardized variances						
BMI at 11–12 y	0.69 (0.56 to 0.84)	0.15 (0.01 to 0.28)	0.15 (0.13 to 0.18)	0.58 (0.44 to 0.74)	0.21 (0.06 to 0.35)	0.21 (0.18 to 0.24)
BMI at 14 y	0.66 (0.52 to 0.82)	0.17 (0.02 to 0.30)	0.16 (0.14 to 0.20)	0.58 (0.44 to 0.75)	0.24 (0.07 to 0.38)	0.18 (0.15 to 0.21)
BMI at 17 y	0.83 (0.72 to 0.86)	0.00 (0.00 to 0.11)	0.17 (0.14 to 0.20)	0.74 (0.56 to 0.81)	0.03 (0.00 to 0.20)	0.23 (0.19 to 0.27)
Non-standardized variances						
BMI at 11–12 y	1.31 (1.06 to 1.59)	0.29 (0.02 to 0.54)	0.29 (0.25 to 0.33)	1.16 (0.87 to 1.48)	0.42 (0.11 to 0.70)	0.41 (0.36 to 0.47)
BMI at 14 y	1.14 (0.90 to 1.41)	0.30 (0.04 to 0.53)	0.28 (0.24 to 0.33)	1.05 (0.79 to 1.36)	0.43 (0.13 to 0.70)	0.32 (0.28 to 0.37)
BMI at 17 y	1.41 (1.20 to 1.54)	0.00 (0.00 to 0.19)	0.28 (0.24 to 0.34)	1.14 (0.86 to 1.30)	0.04 (0.00 to 0.31)	0.35 (0.30 to 0.40)

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