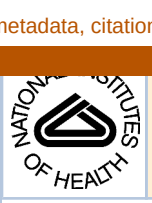

Published in final edited form as:

Obesity (Silver Spring). 2010 July ; 18(7): 1474–1476. doi:10.1038/oby.2009.350.

Genetic Epidemiology of Body Mass Index and Body Mass Change From Adolescence to Young Adulthood

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Abstract

The complex interplay between genes and environment affecting body mass gain over lifecycle periods of risk is not well understood. We use longitudinal sibling cohort data to examine the role of shared household environment, additive genetic, and shared genetic effects on Body Mass Index (BMI) and BMI change. In the National Longitudinal Study of Adolescent Health, siblings and twin pairs sharing households for ≥10 years as adolescents (N=5524; mean=16.5±1.7 years) were followed into young adulthood (N = 4368; mean=22.4±1.8 years). Using a variance component approach, we quantified genetic and household effects on BMI in siblings and non-siblings sharing household environments over time. Adjusting for race, age, sex, and age by sex interaction, we detected a heritability of 0.43±0.05 for BMI change. Significant household effects were noted during the young adulthood time period only (0.11±0.06). We find evidence for shared genetic effects between BMI and BMI change during adolescence [Genetic Correlation (ρ_G)=0.61±0.03] and young adulthood (ρ_G=0.23±0.06). Our findings support a complex etiology of BMI and BMI change.

Introduction

Numerous contributions have been made regarding the overall genetic and environmental influences on obesity at a given time point in life (1), yet little is known about effects over the lifecycle. Family studies characterizing genetic and environmental components of BMI change estimate heritability between 14 and 37%. (2-4) Yet results may not be generalized across the lifecycle, particularly during periods of high risk, such as the transition from adolescence to young adulthood (5). Likewise, the effect of household may vary across the lifecourse (6). In addition, modest correlations between baseline BMI and BMI change in adult twins suggest that there may be some genetic variants for BMI change that are distinct from those affecting BMI level (7,8). We followed an ethnically diverse, sibling cohort to examine the role of shared

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Supplementary Materials Description

The variance component approach we implemented using SOLAR is briefly summarized in the supplementary methods.

Disclosure

The authors declare no conflict of interest.

household environment and additive genetic effects on BMI change from adolescence to adulthood.

Methods and Procedures

Study population

The National Longitudinal Study of Adolescent Health (Add Health) is a nationally representative, longitudinal survey following 20,745 adolescents (Wave I, 1994 to 1995) in grades 7-12 and their parents into adulthood. Wave II (1996, n = 14,438) included Wave I adolescents who had not graduated from high school, including drop-outs. Wave III (2001-2002, n = 15,197) included all located Wave I respondents, aged 18 to 27 years. Survey procedures described elsewhere (9) were approved by the Institutional Review Board, University of North Carolina at Chapel Hill.

Family Subsample

Add Health included a respondent subsample matched with up to five related and non-related adolescents per household (mean, 2.1±0.4 individuals/household across 5524 Wave I respondents living in 2639 households. We limited our sample to 4782 adolescents (in 2302 households) sharing household/physical environments for ≥10 years at Wave I (Figure 1). In Wave III, 4588 participants were surveyed as young adults; 913 individuals (in 449 households) continued living with another survey respondent, excluding participants who were severely disabled (n = 100), pregnant (Wave II, n = 75; III, n = 94), or missing BMI (Wave II, n = 450; III, n = 613). Twin zygosity determined by molecular markers, non-twin sibships classified by self-report (http://www.cpc.unc.edu/projects/addhealth/) (10).

BMI

BMI (kg/m^2) was calculated from measured height and weight, assessed at Waves II and III using standardized procedures. Self-reported height and weight were substituted for those refusing measurement and/or weighing more than scale capacity (Wave II, n = 54; III, n = 155) (5). Obesity was defined as BMI ≥ 95th percentile of the National Center for Health Statistics/ Centers for Disease Control and Prevention reference curves (11) in adolescence and the BMI ≥ 30 cut-point in adulthood (12).

Statistical methods

To identify and evaluate the genetic and environmental contributions to BMI and BMI change we used a variance component approach implemented in SOLAR (13), which is explained in detail in previous publications (14,15) and briefly summarized in the supplementary methods. All models were adjusted for race, age, sex, and age-by-sex interaction.

Results

From adolescence (mean age = 16.5±1.7 years) to young adulthood (mean age = 22.4±1.8 years) BMI increased from 22.9±4.9 kg/m^2 to 26.2±6.2 kg/m^2 and overweight/obesity rose from 11.3% to 21.6%. Mean BMI change was 3.2±3.4 kg/m^2.

Adjusting for race, age, sex, and age by sex interaction, we estimated a heritability of 0.43 ±0.05 for BMI change (Table 1).

Though slightly higher in Whites, heritability was fairly similar across ethnicity. Due to power restrictions, we were only able to interrogate the household effect in the full sample, where significant household effects were noted during young adulthood (Table 2). Moreover, the additive genetic signal was reduced once household variance was incorporated.

Findings suggest shared genetic effects between BMI level and during adolescence (rhoG) =0.61±0.03; *P*=0.001) that weakened in adulthood (rhoG=0.23±0.06; *P*=0.01).

Discussion

We found moderate to strong evidence for the additive effects of genes influencing BMI change in a nationally representative, ethnically diverse sibling cohort of adolescence followed into young adulthood. These heritability estimates are higher than those from other family studies, (2-4) perhaps due to the large variance in BMI change during this critical period of weight gain or to features of our study design, i.e. the sample is primary composed of sibling pairs. The heritability estimates were most similar to those reported by Rice et al, in participants from the Longitudinal Quebec Family Study, where they calculated heritability for BMI change of 37% over a 12-year period. This heritability estimate was mainly driven by correlations between young adult siblings, ranging in age from 19 to 31 years between the two BMI measurements. In comparison to other family studies, this study may have been most similar in age to the Add Health cohort. However, direct comparison of heritability estimates across studies is problematic due to differences in study designs, ascertainment schemes, methods of parameter estimation, and population-specific environmental contributions to the phenotypic variance (16). The vast majority of literature on heritability is in European samples. Taking advantage of our large, ethnically diverse sample, we found that residual heritability was fairly similar across ethnicity, although power limitations precluded estimation of ethnic-specific interactions.

Household effects are attributable to unmeasured non-genetic factors (e.g., dietary or lifestyle factors) that are shared more closely by members of the same (versus different) household (16). We found household effects at young adulthood, but not during adolescence perhaps because dietary and physical activity behaviors of adolescents likely mirror parental and sibling behaviors while they live in the same household (17), but may change as young adults move out and establish their own households. Thus, the differences in household behaviors become more varied as siblings move away from each other and their parents.

Conversely, shared genetic effects between BMI level and change were stronger during adolescence than young adulthood. Research in adult twins similarly shows low genetic correlation between BMI level and change (suggesting little overlap in the genetic variants influencing these phenotypes), which coupled with our findings provide support for distinct genetic effects (7,8).

In summary, our findings suggest that BMI change, particularly in adolescence, may be an important trait for mapping genes related to obesity. In addition, our findings support previous findings of a complex etiology of BMI change, involving genetic ***and*** environmental components.

Acknowledgments

This work was funded by NIH, R01HD057194. This research uses data from Add Health, a program project designed by J. Richard Udry, Peter S. Bearman, and Kathleen Mullan Harris, funded by P01-HD31921 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 17 other agencies. Special acknowledgment is due Ronald R. Rindfuss and Barbara Entwisle for assistance in the original design. Persons interested in obtaining data files from Add Health should contact Add Health, CPC, 123 W. Franklin Street, Chapel Hill, NC 27516-2524 (addhealth@unc.edu). No direct support was received from grant P01-HD31921 for this analysis. We thank Add Health participants, and the collaborators & staff of Add Health.

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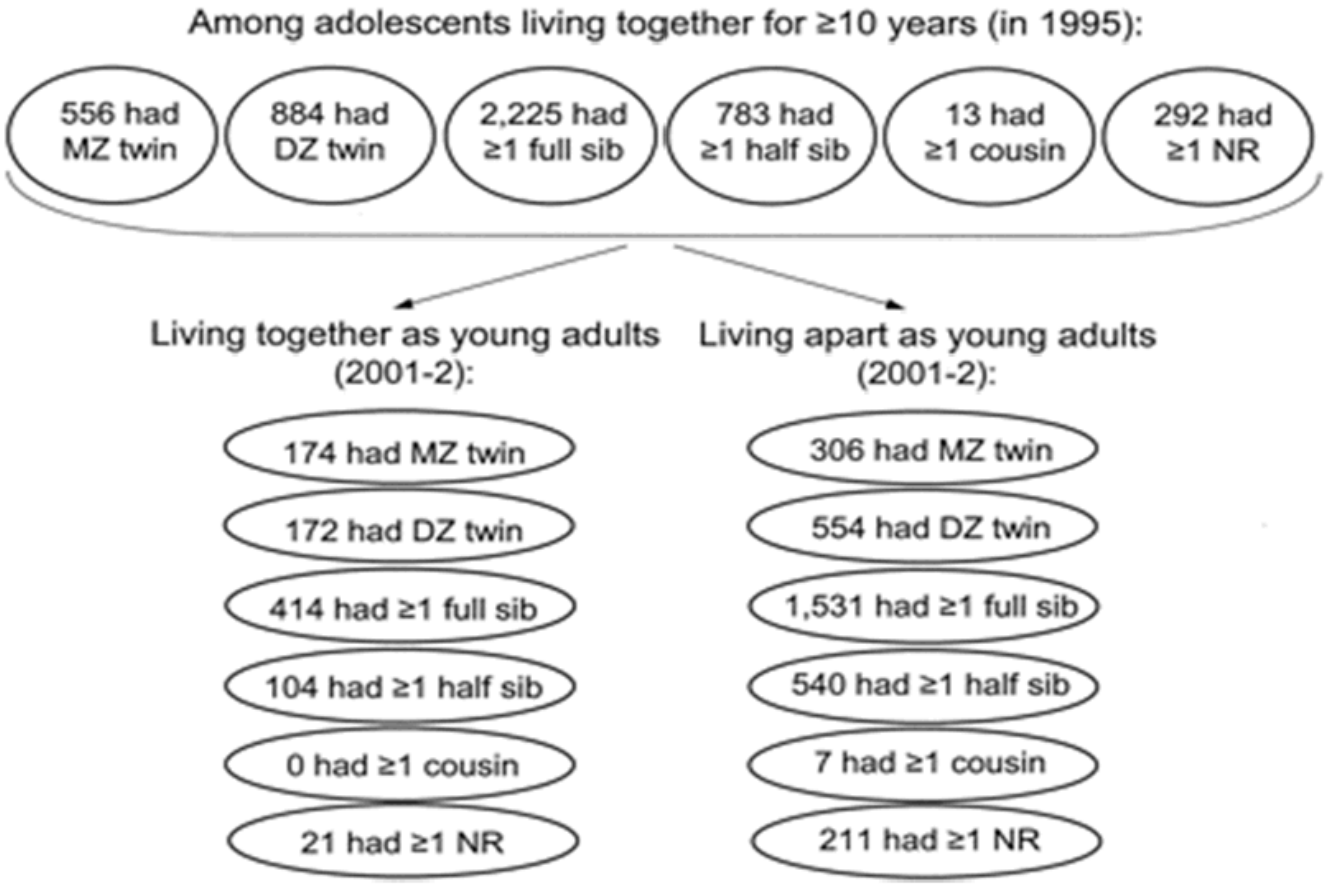

Figure 1.
Shared and non-shared environments among the sibling and household analysis sample of Add Health[a]
[a]Adapted from Nelson et al.,2006: *Obesity* 14(4): 701-709 NR=non-relative

Table 1

Residual Heritability of Body Mass Change in Young Adults: The National Longitudinal Study of Adolescent Health.

	Heritability[a]	*P* value
All Races	0.43 ± 0.05	0.0000001
Whites	0.49 ± 0.07	0.0000001
African Americans	0.42[b]	0.0003
Hispanics	0.39[b]	0.17
Asians	0.39[b]	0.34

[a] After accounting for the effects of age, sex, and age-by-sex interaction.

[b] Standard errors could not be computed.

Table 2

Residual Heritability and Household Effects on Body Mass Change in Add Health Participants

	Heritability	Household Variance
BMI Change and Adolescent Household[a]	0.43 ± 0.05[c]	0.00[d]
BMI Change and Young Adult Household[a]	0.23 ± 0.06 [c]	0.11 ± 0.06[b]

[a] After accounting for the effects of age, sex, and age-by-sex interaction;

[b] $P = 0.02$;

[c] $P < 0.01$;

[d] Estimated on a boundary, standard errors could not be computed.