The genetic architecture of the association between eating behaviors and obesity: combining genetic twin modeling and polygenic risk scores

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ABSTRACT

Background: Obesity susceptibility genes are highly expressed in the brain suggesting that they might exert their influence on body weight through eating-related behaviors.

Objectives: To examine whether the genetic susceptibility to obesity is mediated by eating behavior patterns.

Methods: Participants were 3977 twins (33% monozygotic, 56% females), aged 31–37 y, from wave 5 of the FinnTwin16 study. They self-reported their height and weight, eating behaviors (15 items), diet quality, and self-measured their waist circumference (WC). For 1055 twins with genome-wide data, we constructed a polygenic risk score for BMI (PRSBMI) using almost 1 million single nucleotide polymorphisms. We used principal component analyses to identify eating behavior patterns, twin modeling to decompose correlations into genetic and environmental components, and structural equation modeling to test mediation models between the PRSBMI, eating behavior patterns, and obesity measures.

Results: We identified 4 moderately heritable (h² = 36–48%) eating behavior patterns labeled “snacking,” “infrequent and unhealthy eating,” “avoidant eating,” and “emotional and external eating.” The highest phenotypic correlation with obesity measures was found for the snacking behavior pattern (r = 0.35 for BMI and r = 0.32 for WC; P < 0.001 for both), largely due to genetic factors common to both (16). The pathways through which obesity-associated loci (GWASs) of BMI from Locke et al. (17) identified 97 BMI-associated loci [single nucleotide polymorphisms (SNPs)], but explained <4% of the variance in BMI. A more recent meta-analysis of GWASs by Yengo et al. (18) extended the number of BMI-associated SNPs to 751, explaining 6% of the variance in BMI. Whole-sequence genome data increase the fraction of variance of BMI accounted for by genetic variants, both common and rare, to 40% (18). The pathways through which obesity-associated genetic variants predispose certain individuals to develop obesity are not well understood, but because obesity...
susceptibility genes are highly expressed in the central nervous system (19), they are likely to influence appetite and satiety traits, which therefore represent a plausible behavioral pathway for weight gain (16, 20, 21).

A few earlier studies have focused on the associations between eating behaviors and genetic susceptibility to obesity. Two studies performed in adults have reported that uncontrolled eating and emotional eating mediate the association between a polygenic risk score (PRS) comprising 90 BMI-associated loci and obesity measures (21, 22). A more recent study that used a 97-loci PRS indicated that the genetic susceptibility to obesity is partially mediated by disinhibition and susceptibility to hunger (23). These previous studies have defined genetic susceptibility to obesity based on <100 SNPs that reached genome-wide significance. Khera et al. (24) recently suggested the use of a PRS by incorporating all available information from ≤2.1 million common genetic variants irrespective of genome-wide significance, hence providing a more powerful approach for capturing genetic risk (18). Research has not yet determined the associations between such a whole-genome–based PRS for obesity, eating behavior patterns, and obesity measures. Thus, the aims of this study were to examine whether eating behavior patterns are related to obesity measures, to study whether genetic susceptibility to obesity is mediated by eating behavior patterns in a nationwide setting in Finland using the latest PRS for obesity, and to test these associations using a genetically informative twin design.

Methods

Participants

The data for this study were derived from the longitudinal FinnTwin16 (FT16) cohort including Finnish twins born in 1975–1979 and identified from the population register (n = ∼5600 twin individuals) (25). The FT16 study was targeted to investigate determinants of health-related behaviors, disease risk factors, and chronic diseases in adolescents and young adults. Data from the latest survey in 2010–2012 (wave 5), when the participants were on average 34 y old, were used in the present study. The questionnaire was administered as an internet survey. The invitation was sent to all twins belonging to the original target population, regardless of earlier participation (total n = 4407 twin individuals, response rate 72%, and n = 1055 twin individuals had genome-wide data available). We excluded participants with unknown zygozity, eating styles, diet quality, and BMI. In mediation analyses we excluded twin individuals with missing genome-wide data. In quantitative twin genetic analyses, we excluded those without a co-twin and without information on zygozity, eating styles, and diet quality. The final data (Figure 1) included 3977 twin individuals [527 monoyzogotic (MZ), 470 same-sex dizyogotic (SS-DZ), and 503 opposite-sex dizyogotic (OS-DZ) twin pairs] (Supplemental Table 1A) and 949 twin individuals for mediation analyses (Supplemental Table 1B). Zygosity was derived from questionnaires, based on physical similarity and confusing by others, a method that has shown high reliability in this cohort (26). The data collection was approved by the Ethics Committee of the Central Finland Health Care District (April 20, 2010, Dnro 4/2010).

Measurements

Eating styles and diet quality.

Eating styles were assessed with a 16-item questionnaire modified from Keski-Rahkonen et al. (27). The questionnaire was cross-validated with various established assessment tools—the Three-Factor Eating Questionnaire (28, 29), the Binge Eating Scale (30), and the Eating Disorder Inventory (31)—in a small subsample (n = 42) of FinnTwin16 participants. Subscales of those instruments were significantly correlated with our eating style items except for those describing health-conscious/avoidant eating and 1 item regarding snacking. However, in the study from Keski-Rahkonen et al. (27), health-conscious eating and snacking items had moderate internal consistency (Cronbach α = 0.70 and 0.61, respectively). The participants were asked to select the option that best described their overall eating style (2 items for assessing meal frequency and 2 items for regular eating styles). Another 3 items inquired about health-conscious eating, 1 item about night eating, 1 item about external eating, 2 items about emotional eating, and 5 items about snacking styles with 4 different alternatives: “usually,” “often,” “sometimes,” or “seldom” (32). The item about night eating style was excluded due to a lack of variability in participants’ responses. Dietary intake was assessed by a short FFQ, from which a diet quality score (DQS) was calculated, as previously described (32). The DQS had been previously validated and is associated with obesity measures and eating styles in this cohort (32). The DQS ranges...
Genetics of eating behavior patterns and obesity

FinnTwin16 Study (wave 5)

Twin individuals with data on zygosity
n = 4160

Missing data on diet quality, eating styles or BMI
n = 183

Twin individuals for analyses
n = 3977

Complete twin pairs with data on zygosity
n = 1576 pairs

Missing data on diet quality or eating styles
n = 76 pairs

Complete twin pairs for analyses
n = 1500 pairs

FIGURE 1 Flowchart diagram of participants’ selection.

from 0 to 12 points, with a higher score indicating a better diet quality.

Obesity measures.

Height and weight were self-reported, from which BMI (kg/m²) was calculated. Waist circumference (WC) was self-measured midway between the lowest rib and the iliac crest with a tape. The participants received a tape and instructions by mail on how to self-measure WC. The validity of self-reported height, weight, and WC was previously demonstrated in a subsample of FT16 participants (33).

Genotyping and weighted PRS.

Genotyping was performed in the United States, United Kingdom, and Finland (see Supplemental Methods for more details). Genotyping quality control batches were applied for SNPs [minor allele frequency (MAF)]. First, we removed every genetic variant with a call rate <0.975 (batches 1 and 3) or <0.95 (batch 2). Second, we removed every sample with a call rate <0.98 (batch 1) or <0.95 (batches 2 and 3). Finally, variants were filtered by their MAF <0.01 with Hardy–Weinberg equilibrium P value <1e-06. Samples from all batches were imputed to the Haplotype Reference Consortium release 1.1 reference panel (36).

Prephasing of the data was done with Eagle v2.3 (34) and imputation with Minimac3 v2.0.1 using the University of Michigan Imputation Server (35). Genotypes from all the batches were imputed to the Finnish FINRISK study sample were restricted to the European HapMap3 variants (39) with an MAF >5%. The major histocompatibility complex gene cluster of human chromosome 6 (GRCh37: 6p22.1–21.3) was excluded due to strong LD block. We derived 2 PRSs, 1 for BMI (PRS_{BMI}) and 1 for waist-to-hip ratio (WHR) adjusted for BMI (PRS_{WHR}). The total numbers of genetic variants used for the PRS calculations were 996,919 for BMI and 1,148,565 for WHR adjusted for BMI, with the reweighted effect sizes available from 692,578 and 484,563 samples, respectively (see Supplemental Methods for more details of the different PRSs).

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The PRS_{BMI} explained 8.3% of the variance in BMI in this study sample.

Statistical methods

General characteristics of the study sample are presented as means and 95% CIs for continuous variables and as numbers and percentages for categorical variables. Differences between
men and women were determined using the adjusted Wald test for continuous variables and Pearson $\chi^2$ test for categorical variables.

**Principal component analyses.**

Eating behavior patterns were derived by principal component analyses (PCAs) using 15 eating styles and 1 indicator of diet quality (DQS). Based on eigenvalues $>1.0$ and scree plot analyses, we retained 4 components. We calculated factor loadings after a varimax rotation to simplify and facilitate their interpretability. Factor loadings ($>0.30$) were considered to contribute to the eating behavior pattern and were used to label the 4 components.

**Quantitative genetic analyses.**

We used quantitative genetic twin modeling, based on linear structural equations, to estimate the heritability of eating behavior patterns and obesity measures (40). Classical twin modeling is based on the assumption that MZ twins share virtually the same gene sequence, whereas dizygotic (DZ) twins share, on average, 50% of their genetic variance, like other siblings. Based on these assumptions, genetic variation can be decomposed into additive genetic variation (A), which is the sum of the allelic effects on the phenotype over all relevant loci, and dominance genetic variation (D), including nonadditive genetic effects. Environmental variation can be decomposed into shared environmental variation (C), which includes all environmental factors that make co-twins similar, and nonshared environmental variation (E), which includes all environmental factors that make co-twins dissimilar (as well as measurement error). The expected correlations for additive and dominance genetic effects are both 1 for MZ twins and 0.5 and 0.25 for DZ twins, respectively. By definition, the expected correlations for shared and nonshared environmental effects are 1 and 0, respectively, for both MZ and DZ twins. Before model fitting, we calculated intraclass correlations (ICCs) for MZ, SS-DZ, and OS-DZ twin pairs to estimate the level of within-pair similarity and to provide evidence for the presence of genetic effects (40).

We started the analyses by computing univariate models (41). Because we had information only on twin pairs reared together, we were unable to estimate dominance genetic and shared environmental effects simultaneously. Thus, we first tested whether shared environmental factors and dominant genetic factors were present to explain the variation in eating behavior patterns and obesity measures by comparing the ACE and ADE models with the AE model. No evidence of C or D was found; hence, a more parsimonious additive genetic/nonshared environment (AE) model was used in all further genetic twin modeling.

After the univariate models, we calculated correlations between eating behavior patterns and obesity using Pearson partial correlations. Then we used the bivariate Cholesky decomposition to examine the extent to which genetic and nonshared environmental effects underlie the observed correlation between the 2 traits. In addition, this bivariate design allowed us to derive additive genetic ($r_g$) and shared environmental ($r_e$) correlations (40). All analyses were adjusted for age and sex.

**Structural equation modeling.**

Structural equation modeling (SEM) analyses were conducted to identify potential mediation models between the PRSs (PRSBMI and PRSWHR) and obesity measures through eating behavior patterns (42). To control for age, sex, and population stratification, we regressed all of the variables on age, sex, and genetic principal components and then used the residuals in the SEM analyses. Genetic principal components came from the merged raw phenotype data of all samples, to detect any population stratification due to systematic ancestry differences (43). Analyses with PRSWHR were only controlled for age and sex. Total effects ($c + ab$), direct effects ($c$), and indirect or mediation effects ($ab$) were calculated to show how much of the association between the PRS and the obesity measure was mediated by the different eating behavior patterns. Bias corrected estimates and 95% CIs were calculated using the bootstrapping approach with 1000 draws. All of the models were estimated for every eating behavior pattern and for both obesity measures using both PRSs, and the results are presented as total, direct, and indirect effects. We added interaction terms to test whether the mediation models were similar in men and women. Because some of the interaction terms were significant ($P < 0.05$), we present the mediation models separately by sex in Supplemental Table 3.

When analyzing twins as individuals, the effect of the twin pair clustering was taken into account in SEs yielded by cluster variance estimators, which were robust to nonindependent observations within families (44). The descriptive statistics, PCAs, ICCs, Pearson partial correlations, and SEM were conducted by using Stata software (release 14.1; StataCorp). Quantitative genetic analyses were carried out with the OpenMx package (version 2.14.11) of R statistical software (R Project for Statistical Computing) (45). A $P$ value $<0.05$ was considered as the level of significance.

**Results**

**General characteristics of the study sample**

Table 1 shows the descriptive characteristics of the study sample. Approximately 56% of the study sample were women and 33% were MZ twins. The participants had, on average, a BMI of 24.8 and a WC of 86.1 cm. The mean DQS was 7 points from a maximum of 12 points. Women had a lower BMI and WC, but they were abdominally obese more often than men. Women had a higher diet quality than men (mean DQS: 7.4 for women and 6.4 for men; $P < 0.001$). There were no differences between men and women with respect to standardized PRSs. Supplemental Table 1A shows the descriptive statistics by zygosity, and Supplemental Table 1B shows the descriptive statistics for the subsample used in the mediation analyses.

**Eating behavior patterns**

Results of the PCAs of eating behavior patterns, which included 15 questions on eating styles and the DQS, are shown in Table 2. The resultant eating behavior patterns were labeled “snacking,” “infrequent and unhealthy eating,” “avoidant eating,” and “emotional and external eating.” These 4
components together explained ~56% of the variance in eating styles and diet quality.

**ICCs and heritability estimates**

ICCs were higher in MZ twins than DZ twins, indicating the presence of genetic influences (Supplemental Table 2). Heritability estimates of eating behavior patterns and obesity measures are shown in **Figure 2**. The variation in eating behavior patterns and obesity measures was due to both additive genetic and non-shared environmental factors. Eating behavior patterns showed moderate heritability estimates, ranging from 36% to 48%. As expected, the heritability estimates for BMI and WC were high (76% and 62%, respectively). When stratifying the analyses by sex, heritability estimates were slightly higher in women than in men, although CIs were overlapping (Supplemental Figure 1).

**TABLE 1** General characteristics of the study sample

| Characteristics                                      | Overall (n = 3977) | Men (n = 1732) | Women (n = 2245) | P value |
|------------------------------------------------------|--------------------|----------------|------------------|---------|
| Monozygotic twins, n (%)                             | 1298 (32.6)        | 505 (29.2)     | 793 (35.3)       | 0.001   |
| Same-sex dizygotic twins, n (%)                      | 1272 (32.0)        | 603 (34.8)     | 669 (29.8)       |         |
| Opposite-sex dizygotic twins, n (%)                  | 1407 (35.4)        | 624 (36.0)     | 783 (34.9)       |         |
| Age, y, mean (95% CI)                                | 34.1 (34.1, 34.1)  | 34.1 (34.1, 34.2) | 34.1 (34.0, 34.1) | 0.4     |
| BMI, kg/m², mean (95% CI)                            | 24.8 (24.6, 24.9)  | 25.7 (25.5, 25.9) | 24.0 (23.8, 24.2) | <0.001  |
| WC, cm, mean (95% CI)                                | 86.1 (85.6, 86.5)  | 92.1 (91.6, 92.7) | 81.2 (80.7, 81.8) | <0.001  |
| Abdominal obesity (women >88 cm; men >102 cm), n (%) | 771 (20.1)         | 268 (15.8)     | 503 (23.6)       | <0.001  |
| Diet quality score, mean (95% CI)                    | 415 (10.4)         | 186 (10.7)     | 229 (10.2)       | 0.6     |
| Standardized PRSBMI, mean (95% CI)                   | 6.6e− 10 (−0.1, 0.1) | 0.0 (−0.1, 0.2) | 0.0 (−0.1, 0.1)  | 0.4     |
| Standardized PRSWHR, mean (95% CI)                   | 1.2e− 09 (−0.1, 0.1) | 0.0 (−0.1, 0.2) | 0.0 (−0.1, 0.1)  | 0.4     |

1Differences between men and women, P values, were determined by the adjusted Wald test for continuous variables and Pearson χ² test for categorical variables and corrected for the clustering of twin pairs by survey methods. PRS, polygenic risk score; WC, waist circumference; WHR, waist-to-hip ratio.

2Sample size smaller due to missing genotypes. Overall sample size for WC and abdominal obesity n = 3832; overall sample size for standardized PRSBMI and standardized PRSWHR n = 949.

**TABLE 2** Eating behavior patterns and factor loadings in varimax-rotated principal components

| Variables                                      | Snacking | Infrequent and unhealthy eating | Avoidant eating | Emotional and external eating |
|------------------------------------------------|----------|---------------------------------|-----------------|-------------------------------|
| Eigenvalue                                     |          |                                 |                 |                               |
| Variable coding                                |          |                                 |                 |                               |
| Diet quality score                             | 4.00     | 2.43                            | 1.38            | 1.09                          |
| Percentage variance explained                  | 16.6      | 13.6                            | 12.8            | 12.7                          |

**Associations between eating behavior patterns and obesity measures**

All of the 4 eating behavior patterns were positively correlated with obesity measures, except for the avoidant eating behavior pattern, which was not correlated with BMI, and the infrequent and unhealthy eating behavior pattern, which was not correlated with WC adjusted for BMI (Table 3). For both BMI and WC, the highest phenotypic correlations were observed for the snacking behavior pattern \( r_p = 0.35 \) and \( 0.32, \) respectively, and the emotional and external eating behavior pattern \( r_p = 0.26 \) and \( 0.23, \) respectively. Thus, we decomposed these 4 correlations into genetic and environmental components (Figure 3A, B). Higher scores on the snacking and avoidant eating behavior patterns were associated with a higher WC adjusted for BMI, but these associations were very weak (Table 3). Therefore, we did not decompose these correlations into genetic and environmental components.
FIGURE 2 Proportion of variation of the eating behavior patterns and obesity measures explained by additive genes (A) and nonshared environmental factors (E). The numbers within the bars are means and 95% CIs; n = 3000. WC, waist circumference.

Figure 3A shows the path diagram of the bivariate Cholesky model decomposing the correlations between the snacking behavior pattern and obesity measures (BMI and WC), and Figure 3B shows the corresponding results for the emotional and external eating behavior pattern and obesity measures (BMI and WC). For the snacking and emotional and external eating behavior patterns, the additive genetic correlations with both obesity measures were higher than the nonshared environmental correlations. The proportion of the covariance explained by genes was 75% (95% CI: 61, 88%) and 71% (95% CI: 58, 93%) for the snacking behavior pattern and BMI and WC, respectively; and 75% (95% CI: 55, 87%) and 64% (95% CI: 44, 85%) for the emotional and external eating behavior pattern and BMI and WC, respectively.

TABLE 3 Association between eating behavior patterns and obesity measures

| Obesity measures | Eating behavior patterns | Pearson partial correlation | r  | P value |
|------------------|-------------------------|----------------------------|----|---------|
| Body mass index  | Snacking                | 0.35                       | 0.35 | <0.001  |
|                   | Infrequent and unhealthy eating | 0.12                     | 0.12 | <0.001  |
|                   | Avoidant eating         | 0.01                       | 0.01 | 0.8     |
|                   | Emotional and external eating | 0.26                    | 0.26 | <0.001  |
| Waist circumference| Snacking                | 0.32                       | 0.32 | <0.001  |
|                   | Infrequent and unhealthy eating | 0.11                     | 0.11 | <0.001  |
|                   | Avoidant eating         | 0.04                       | 0.04 | 0.02    |
|                   | Emotional and external eating | 0.23                    | 0.23 | <0.001  |
| Waist circumference| Snacking                | 0.06                       | 0.06 | 0.001   |
| adjusted for BMI  | Infrequent and unhealthy eating | 0.02                     | 0.02 | 0.2     |
|                   | Avoidant eating         | 0.07                       | 0.07 | <0.001  |
|                   | Emotional and external eating | 0.03                    | 0.03 | 0.09    |

Eating behavior patterns as mediators of genetic susceptibility to obesity

As expected, the PRS BMI was positively associated with BMI and WC. Among the 4 eating behavior patterns, only the snacking and the infrequent and unhealthy eating behavior patterns significantly mediated the association between the PRS BMI and both obesity measures (BMI and WC) (Table 4). However, the infrequent and unhealthy eating behavior pattern mediated this association to a much weaker extent (see Supplemental Figure 2 for more details). The emotional and external eating behavior pattern only mediated the association between the PRS BMI and BMI.

A more detailed description of the pathways of the mediation model for the snacking behavior pattern is shown in Figure 4. The PRS BMI was positively associated with the snacking behavior pattern, indicating that individuals with a higher PRS BMI are more susceptible to snacking (a: β = 0.15 for BMI and β = 0.14 for WC), and a higher loading on the snacking behavior pattern was associated with a higher BMI and WC (b: β = 0.38 and 0.32,
FIGURE 3  (A) Path diagram of a bivariate Cholesky model for 1 member of a twin pair. Additive genetic ($r_a$) and nonshared environmental ($r_e$) correlations between BMI/WC and the snacking behavior pattern and 95% CIs. The covariance of the traits was decomposed into additive genetic (A) and nonshared environmental (E) effects. All models were adjusted for age and sex; $n = 527$ monozygotic, 470 same-sex dizygotic, and 503 opposite-sex dizygotic pairs. (B) Path diagram of a bivariate Cholesky model for 1 member of a twin pair. Additive genetic ($r_a$) and nonshared environmental ($r_e$) correlations between BMI/WC and the emotional and external eating behavior pattern and 95% CIs. The covariance of the traits was decomposed into additive genetic (A) and nonshared environmental (E) effects. All models were adjusted for age and sex; $n = 527$ monozygotic, 470 same-sex dizygotic, and 503 opposite-sex dizygotic pairs.

The PRSBMI was not associated with WC adjusted for BMI (data not shown). The associations between the PRS BMI and obesity measures are shown in Table 4. Our results are novel because, to the best of our knowledge, research to date has not yet employed polygenic risk and classical twin modeling simultaneously to study the genetic architecture underlying eating behavior patterns and obesity.

Discussion

In this cross-sectional study of healthy young adults, we showed that the association between the most recent PRSBMI and obesity measures was partly mediated by the snacking behavior pattern in men and women and to a lesser extent by the infrequent and unhealthy eating behavior pattern in men. The association between the PRSBMI and BMI was also partly mediated by the emotional and external eating pattern. In the twin modeling, the associations between the snacking and the emotional and external eating behavior patterns and BMI and WC were largely explained by genetic factors, supporting the inference that the snacking and the emotional and external eating behavior patterns and obesity share a common underlying genetic architecture. Another important finding was that eating behavior patterns were moderately heritable, with the remaining variance accounted for by nonshared environmental factors.

Our results are novel because, to the best of our knowledge, research to date has not yet employed polygenic risk and classical twin modeling simultaneously to study the genetic architecture underlying eating behavior patterns and obesity. Because the mediation by snacking has not been reported previously, it is difficult to compare our results with the previous literature. A recent review from Vainik et al. (46) supported that uncontrolled eating might involve other eating behavior constructs, which include the overeating behavior. Our snacking behavior pattern had a high loading on alternating restriction and overeating style, somewhat similar to these previous constructs.
TABLE 4  Structural equation modeling of the PRSBMI and obesity measures

| Mediation model through snacking | BMI (n = 949) | WC (n = 874) |
|----------------------------------|---------------|---------------|
| Total effect of PRSBMI           | 0.29 (0.20, 0.38) | 0.24 (0.15, 0.32) |
| Direct effect of PRSBMI          | 0.23 (0.16, 0.31) | 0.19 (0.12, 0.26) |
| Indirect effect (via snacking) of PRSBMI on obesity measures | 0.06 (0.02, 0.09) | 0.05 (0.02, 0.08) |
| Percentage mediation             | 20.7          | 20.8          |
| Mediation model through infrequent and unhealthy eating | Total effect of PRSBMI | 0.29 (0.20, 0.38) | 0.24 (0.15, 0.32) |
| Direct effect of PRSBMI          | 0.28 (0.20, 0.36) | 0.23 (0.15, 0.31) |
| Indirect effect (via infrequent and unhealthy eating) of PRSBMI on obesity measures | 0.01 (0.00, 0.02) | 0.01 (0.00, 0.02) |
| Percentage mediation             | 3.4           | 4.2           |
| Mediation model through avoidant eating | Total effect of PRSBMI | 0.29 (0.20, 0.38) | 0.24 (0.15, 0.32) |
| Direct effect of PRSBMI          | 0.29 (0.21, 0.38) | 0.24 (0.16, 0.32) |
| Indirect effect (via avoidant eating) of PRSBMI on obesity measures | 0.00 (−0.01, 0.00) | 0.00 (−0.01, 0.00) |
| Percentage mediation             | —             | —             |
| Mediation model through emotional and external eating | Total effect of PRSBMI | 0.29 (0.20, 0.38) | 0.24 (0.15, 0.32) |
| Direct effect of PRSBMI          | 0.26 (0.19, 0.34) | 0.22 (0.15, 0.29) |
| Indirect effect (via emotional and external eating) of PRSBMI on obesity measures | 0.03 (0.00, 0.05) | 0.02 (0.00, 0.04) |
| Percentage mediation             | 10.3          | —             |

1 Standardized regression coefficients (β) and 95% CIs. All models were adjusted for age, sex, and genetic principal components, and clustering was taken into account in all analyses. PRSBMI, polygenic risk score for BMI; WC, waist circumference.

Our results are largely consistent with other studies using a PRSBMI based on <100 SNPs, that have previously reported mediation by undesirable eating behavior traits (21–23). In line with our findings, 2 previous studies have shown that the association between a 90-loci PRS for obesity and obesity measures was partially mediated by uncontrolled eating and emotional eating (21, 22). A more recent study reported similar results for disinhibition and susceptibility to hunger, a behavior similar to uncontrolled eating, as a mediator of the genetic susceptibility to obesity (23). Emotional eating was identified as a mediator of the association between a 90-loci PRS for obesity and BMI and WC in the study by Konttinen et al (21). In that study, the indirect association had a β coefficient of 0.02, and the total effect was β = 0.14 and 0.17 for BMI and WC,

![FIGURE 4](https://academic.oup.com/ajcn/article-abstract/doi/10.1093/ajcn/nqaa181/5873353/28July2020)
respective large difference in the percentage of variance explained.

They provide more evidence for the genetic contribution.

They are highly expressed in the adipose tissue instead of the brain.

In line, in the present study, the PRS BMI was not associated with WC adjusted for BMI. Further, eating behavior patterns did not mediate the associations between the PRS WHR and any of the obesity measures.

In the present study, we found that most of the eating behavior patterns were significantly associated with obesity measures, similarly to previous studies. The strongest associations were seen with the snacking behavior pattern and the emotional and external eating behavior pattern, and genetic factors were largely underlying these associations. These findings accord with other studies on other eating behavior traits, such as that by Konttinen et al., who showed that the associations between uncontrolled eating and BMI as well as emotional eating and BMI are mostly explained by genetic factors. Similarly, twin studies investigating the intake of unhealthy foods and beverages, such as fast food and soda, have shown associations with BMI—which are largely explained by genetic factors common to both. Therefore, together with previous research, our results suggest that eating behavior patterns share a common genetic liability with obesity measures.

Eating behavior patterns were moderately heritable, suggesting that they are influenced by both genetic and environmental factors. In general, our heritability estimates of eating behavior patterns appeared to be somewhat lower than those measured with the Three-Factor Eating Questionnaire. In the present study, we found that the emotional and external eating behavior pattern was moderately heritable, similar to the female Finnish sample from Keski-talo et al. Another study showed heritability estimates of approximately 32% for restrained eating, somewhat similar to avoidant eating in our study, which included avoiding greasy meals and avoiding calories eating style. Our heritability estimates for BMI are consistent with a large-scale meta-analysis and pooled analyses on BMI.

Previous research suggests that genetic factors from heritability estimates provide more evidence for the genetic contribution to obesity susceptibility than genetic variants from GWASs, due to the large difference in the percentage of variance explained between them. Twin studies have demonstrated that a large proportion of the variance in BMI as well as appetitive traits is explained by genetic factors in childhood and adulthood. GWASs have recently increased the knowledge base of common genetic variants associated with obesity, and the PRS used in this study explained 3 times as much of the variance than the PRS reported in previous studies.

In summary, based on the most recent and comprehensive PRS to date, our results strongly suggest that obesity susceptibility genes influence eating behavior patterns and obesity traits consequently.

Our study has several potential limitations. The main limitation is its cross-sectional design; we therefore cannot confirm the causal directions of the relations between eating behavior patterns and obesity measures. However, a previous longitudinal study tested the reciprocity between restrained eating and BMI and WC to determine their potential relations, and they indicated that restrained eating was a marker for previous weight gain instead of a trigger of future weight gain. Future research is needed to carefully test the direction of these relations in a longitudinal design. Despite this, the key question of this study was to examine the genetic architecture underlying obesity measures and eating behavior patterns. We focused on the role of genes rather than the causal associations between obesity measures and eating behavior patterns. Furthermore, the eating styles questionnaire used in this study is a short tool, specifically developed for the FT16 cohort, and therefore is less detailed than other well-established long questionnaires. In this study, we were interested in the overall eating style of the study participants rather than the cognitive aspects of eating and eating behaviors that are assessed by the Three-Factor Eating Questionnaire, used in previous similar studies. Moreover, previous studies that have used this questionnaire in the same cohort have shown associations between these eating styles with obesity as well as diet quality. As in all studies with self-reported data, a further limitation of this study is that eating styles, diet quality, and obesity measures were self-reported by the participants, therefore misreporting might have occurred, especially in women and obese people, because they tend to underreport nutrient intakes and behaviors considered unhealthy. Finally, the generalizability of these results is subject to certain limitations because we used a Finnish cohort of young adults with European ancestry. Further studies are needed to test the generalizability of these results in other non-Westernized populations.

Our study has some important strengths. To our knowledge, this is the first study in adults that tested whether the genetic susceptibility to obesity is mediated by eating behaviors by using a PRS that included almost 1 million SNPs representing the whole genome. We included a combination of twin modeling with GWASs analyses based on very different underlying assumptions. The robustness of our results based on these different methods provides further evidence on the common genetic background of eating behaviors and obesity measures. Finally, the inclusion of diet quality in addition to eating behavior patterns allowed us to assess an additional aspect of diet.

In conclusion, our findings support that eating behavior patterns are moderately heritable. Snacking, and to a lesser extent infrequent and unhealthy and emotional and external eating behavior patterns, share a common genetic liability with obesity measures. Obesity prevention efforts might benefit from focusing on eating behavior change, particularly in genetically susceptible individuals. Future longitudinal and intervention studies will be beneficial to understand how eating behavior patterns and genetic susceptibility to obesity impact life-long weight outcomes.
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