GENDER DIFFERENCES IN THE GENETICS OF DISORDERED EATING AND BODY MASS INDEX

Unique and Shared Etiology

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Sammanfattning:

We assessed the heritability of disordered eating and Body Mass Index (BMI) in a population-based sample of 8,033 Finnish twins and their siblings (age 18-49). Women displayed more disordered eating and had lower mean BMI than men. Disordered eating was positively associated with BMI. Univariate model fitting showed that additive genetic effects accounted for 50% of the variance in disordered eating in women and 62% in men. Unique environmental effects explained the remaining variance. Individual variance in BMI was also principally explained by genetic effects, with estimates of 80% for women and 78% for men. Gender differences in the strenght of genetic effects were tested, yielding significant differences in BMI but not in disordered eating. Furthermore, we tested qualitative gender differences in genetic etiology and found that the genes that contribute to disordered eating and BMI in women were only partly the same as those contributing to disordered eating and BMI in men. Bivariate model fitting was used to explore the possible shared genetics of disordered eating and BMI. The genetic correlation between disordered eating and BMI was .47 for women and .69 for men. The environmental correlation was .19 for women and .17 for men. All of the correlations were significant. In conclusion, the results indicate that disordered eating and body mass index are highly heritable and that they have a significant shared genetic background, but also that there are gender differences in the genetics of both traits.

Nyckelord: behavior genetics, body mass index, disordered eating, twin study, heritability	
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Sammanfattning:

Målet med denna tvillingstudie var att undersöka ärftligheten hos stört ätbeteende och Body Mass Index (BMI) i ett populationsbaserat sampel bestående av 8 033 finska tvillingar och deras syskon (ålder 18-49). Kvinnor uppvisade mer stört ätbeteende än män, och deras BMI var i medeltal lägre än männens. Stört ätbeteende och BMI hade en positiv association. I de univariata genetiska analyserna framkom att 50 % av den individuella variationen i stört ätbeteende hos kvinnor och 62 % av den individuella variationen i stört ätbeteende hos män berodde på genetiska effekter. Resten av variationen förklarades av unika omgivningsfaktorer. Individuell variation i BMI förklarades också huvudsakligen av genetiska effekter (kvinnor: 80 %; män: 78 %), och även där stod unika omgivningfaktorer för den övriga variationen. Signifikanta könsskillnader i storleken av de genetiska effekterna bakom BMI hittades. Inga kvantitativa skillnader i ärftligheten av stört ätbeteende hittades. Generna som påverkar stört ätbeteende respektive BMI hos kvinnor var delvis andra än de som påverkar stört ätbeteende och BMI hos män. En bivariat modell testades för att utreda ifall generrna som påverkar stört ätbeteende delvis är desamma som generna som påverkar BMI. Den genetiska korrelationen mellan stört ätbeteende och BMI var ,47 för kvinnor och ,69 för män. Omgivningskorrelationerna var ,19 för kvinnor och ,17 för män.

Sammanfattningsvis visar resultaten på att såväl stört ätbeteende och BMI är ärftliga, och att de påverkas delvis av samma uppsättning gener. Dessutom fanns det könskillnader i den genetiska etiologin hos båda egenskaper.

Nyckelord: beteendegenetik, body mass index, ärftlighet, tvillingstudier, stört ätbeteende	
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Table of Contents

Introduction

Eating disorders are mental illnesses characterized by major disturbances in eating attitudes and behaviors (American Psychiatric Association, 2000). The current *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV; American Psychiatric Association [APA], 2000) recognizes two specific types of eating disorders: *anorexia nervosa* and *bulimia nervosa*. The main characteristic of anorexia nervosa is the refusal to maintain one's body weight above a minimum level for normal weight. The principal symptoms of bulimia nervosa are recurring episodes of binge-eating and subsequent compensatory behaviors, such as self-induced vomiting or abuse of laxatives (APA, 2000). Severe eating disturbances that do not adhere to the criteria of anorexia nervosa or bulimia nervosa are given the residual diagnosis *eating disorder not otherwise specified* (EDNOS; APA, 2000).

Eating disorders typically appear during puberty or young adulthood, and they are more prevalent in women and girls than in men and boys (APA, 2000; Hoek, 2006; Fernández, Labrador, & Raich, 2005; Hudson, Hiripi, Pope, & Kessler, 2007; Isomaa, 2011; Kjelsås, Bjørnstrøm, & Götestam, 2003). Eating disorders are most prevalent among adolescents, and are assumed to be rare in adults (Croll, Neumark-Sztainer, Story, & Ireland, 2002; Isomaa, 2011; Kelly-Weeder, 2011; Striegel-Moore & Bulik, 2007). Eating disorders are also partially culture-bound, as anorexia nervosa is less prevalent and bulimia nervosa is virtually non-existent in non-Westernized societies (Keel & Klump, 2003). The lifetime prevalence of anorexia nervosa is approximately 0.5% in women (APA, 2000), and 0.3% in men (Hudson et al., 2007). The lifetime prevalence of bulimia nervosa is 1-3% for women (APA, 2000) and 0.5% for men (Hudson et al., 2007). EDNOS is the most common of all eating disorders with a lifetime prevalence of 3.5% in women and 2.0% in men (Hudson et al., 2007; Fernández, Labrador, & Raich, 2005; Kjelsås, Bjørnstrøm, & Götestam, 2003; Machado, Machado, Gonçalves, & Hoek, 2007; Thomas, Vartanian, & Brunell, 2009). The relatively high prevalence of EDNOS is probably due to its more inclusive criteria.

Besides the significant gender differences in the prevalence of clinical cases, there are also significant gender differences in the sub-clinical display of disordered eating. In general, women exhibit more disordered eating than men on almost all points and in almost all studies. The disordered eating behaviors which are clearly more prevalent among women include drive for thinness, dieting for weight control, taking diet pills, being dissatisfied with one's weight, binge eating, fasting, and vomiting after meals (Anderson & Bulik, 2004; Croll,

Neumark-Sztainer, Story, & Ireland, 2002; Jacobi, Hayward, de Zwaan, Kraemer, & Agras, 2004; Kelly-Weeder, 2011; Lewinsohn, Seeley, Moerk, & Striegel-Moore, 2002; Pritchard, 2008; Tamim et al., 2006). These behaviors are much less common among men. In contrast, men report doing more exercise for weight control (Anderson & Bulik, 2004; Lewinsohn et al., 2002; Striegel-Moore et al., 2009).

Although the lifetime prevalence of eating disorders is low, eating disorders are severely disabling and have one of the highest medical complication rates found in psychiatric illnesses (Klump, Bulik, Kaye, Treasure, & Tyson, 2009). There are even studies indicating that anorexia nervosa has a higher standardized mortality rate than any other psychiatric disorder (Klump, Bulik et al., 2009). Also, eating disorders are stable (Fichter & Quadflieg, 2007). For instance, 50% of patients with anorexia nervosa and 25% of patients with bulimia nervosa or EDNOS still fulfill diagnostic criteria ten years after receiving treatment (Keel & Brown, 2010). In addition, up to half of anorexia nervosa and bulimia nervosa cases turn into EDNOS before complete remission from disordered eating is achieved (Keel & Brown, 2010; Tozzi et al., 2005). Remission rates for single diagnoses must therefore be interpreted with caution. In other words, eating disorders are not only potentially fatal and seriously disabling illnesses, but recovering from them is both difficult and time-consuming.

As a result of diagnostic overlap and crossover, a problem that often arises in eating disorders research is that the diagnostic criteria fail to result in clearly defined subgroups or to account for changing symptomatology over the course of the disease. Subsequently, the diagnostic criteria remain the subject of extensive debate (Striegel-Moore & Bulik, 2007). According to Monteleone and Maj (2008), the heterogeneity and overlap in eating disorders may well be the prime reason for genetic etiology research having lead to contradictory and non-conclusive results. Therefore, it is important to not only study the genetics of disordered eating through strictly studying the existing clinical diagnostic groups, but to operationalize disordered eating in other ways as well. As an example of this, studies such as the present one use the broader category of disordered eating.

Assessing the Etiology of Disordered Eating

The etiology of disordered eating is likely to be multifactorial, meaning that several components result in individual differences in disordered eating. These factors include genetic, biological, and temperamental vulnerabilities, which all interact with environmental circumstances. These factors together determine the final phenotype of disordered eating

(Klump, Bulik et al., 2009). The environmental circumstances that affect disordered eating include traumatic childhood experiences, lack of supportive parenting, vast exposure to thin bodies through mass media, and repeated exposure to teasing and negative comments about shape, weight, and eating (Benas & Gibb, 2008; Jacobi et al., 2004; Kim, Heo, Kang, Song, & Treasure, 2010; López-Guimerà, Levine, Sánchez-Carracedo, & Fauquet, 2010; Moriarty & Harrison, 2008; Smyth, Heron, Wonderlich, Crosby, & Thompson, 2008). The extent of their role in relation to the role of genetic effects is what heritability studies try to determine.

Heritability can be measured through adoption studies and twin studies. There is only one adoption study on disordered eating done so far (Klump, Suisman, Burt, McGue, & Iacono, 2009). Its results indicated strong heritability (59-82%), but the sample consisted only of women. Several twin studies estimating the heritability of disordered eating have been made as well, but they have used mainly female adolescent samples. These studies have found moderate to strong genetic effects ranging from 28% to 88% (Bulik, Sullivan, & Kendler, 2000; Jacobi et al., 2004; Javaras et al., 2008; Klump, Bulik et al., 2009; Striegel-Moore & Bulik, 2007), with bulimic symptoms showing stronger heritability in most cases. Also, the studies made so far have found unique environment (i.e. environmental factors that make siblings less similar) to be more influential than shared environment (i.e. environmental factors that add to the similarity in siblings). However, results have been too inconsistent to rule out shared environment as a factor in the development of disordered eating.

Besides the heritability studies on the broader category of disordered eating, characteristic symptoms of disordered eating have been also studied individually. Several of them have appeared to be moderately or even strongly heritable. These include binge eating, restrained eating, and self-induced vomiting (Bulik, Sullivan, Wade, & Kendler, 2000; Mitchell et al., 2011; Munn et al., 2010; Schur, Noonan, Polivy, Goldberg, & Buchwald, 2009). Similarly, related attitudes such as body dissatisfaction, drive for thinness, eating concerns, and concerns with weight and shape are moderately heritable (Keski-Rahkonen et al., 2005; Munn et al., 2010; Rutherford, McGuffin, Katz, & Murray, 1993; Slof Op 't Landt et al., 2008; Spanos, Burt, & Klump, 2010). Taken together, these observations suggest that there is an genetic component behind disordered eating.

Even though the body of heritability research on disordered eating is already vast, the research still lacks extensive and conclusive knowledge on genetic effects on the disordered eating of men. Also, knowledge on whether men's disordered eating has a similar genetic etiology as that of women is still unclear. We found ten studies assessing the genetics of

disordered eating in men (Baker et al., 2009; Eiben, 2007 (as cited in Baker et al., 2009); Keski-Rahkonen, Bulik et al., 2005; Keski-Rahkonen, Neale et al., 2005; Reichborn-Kjennerud et al., 2003; Reichborn-Kjennerud, Bulik, Kendler, et al., 2004; Reichborn-Kjennerud, Bulik, Tambs, & Harris, 2004; Slane, Burt, & Klump, 2007 as as cited in Baker et al., 2009; Slof Op 't Landt et al., 2008; Tholin, Rasmussen, Tynelius, & Karlsson, 2005), of which nine had a female comparison group. The results of these studies showed some discrepancies. For instance, one study found no genetic effects in disordered eating among men (Keski-Rahkonen, Bulik et al., 2005), whereas another found strong genetic effects (Tholin et al., 2005). Despite these inconsistent results, a majority of the studies indicated that disordered eating in men is heritable.

We found only six studies that assessed gender differences in the heritability of disordered eating (Baker et al., 2009; Javaras et al., 2008; Reichborn-Kjennerud et al., 2003; Reichborn-Kjennerud, Bulik, Kendler et al., 2004; Reichborn-Kjennerud, Bulik, Tambs, & Harris, 2004; Slane et al., 2007, as cited in Baker et al., 2009). Results were inconsistent, but at least qualitative gender-specific effects for binge-eating (Reichborn-Kjennerud et al., 2003) have been found, indicating that its genetic risk factors are not entirely the same for men and women. Another study by Slane et al. (as cited in Baker et al., 2009) yielded quantitative gender differences in body dissatisfaction, indicating that women's body dissatisfaction was more genetically determined than men's. Quantitative differences in the disordered eating were also found by Baker et al. (2009), indicating that men's vulnerability to disordered eating is in fact more genetically influenced than women's. In the Baker et al. study, however, the individual symptoms of body dissatisfaction and drive for thinness were more genetically determined for women than for men. The other studies yielded no differences (Javaras et al., 2008; Reichborn-Kjennerudd, Bulik, Tambs, & Harris, 2004; Schur, Noonan, Polivy, Goldberg, & Buchwald, 2009), rendering the pool of results inconsistent. It is therefore clear that more research is needed in order to clarify whether there are differences in the genetic risk factors for disordered eating.

The Association Between Disordered Eating and Body Mass Index

Body Mass Index (BMI) is a measure of the weight-to-height proportionality of a person, and is widely used as a way to define underweight and overweight (World Health Organization, 2011a). BMI is a widely used in clinical work and in research, and it functions well for distinguishing normal weight from health-adverse overweight in most people (World Health Organization, 2011a). Typically, women have a lower mean BMI than men in both

Finland (Helakorpi, Paavola, Prättälä, & Uutela, 2009; Korkeila, Kaprio, Rissanen, & Koskenvuo, 1995) and in the world in general (Schousboe et al, 2003). BMI has also been discovered to increase with age (Korkeila et al., 1995).

BMI is strongly influenced by genetics (Klump, McGue, & Iacono, 2000; Lajunen et al., 2009; Mustelin, Silventoinen, Pietiläinen, Rissanen, & Kaprio, 2009; Ortega-Alonso, Sipilä, Kujala, Kaprio, & Rantanen, 2009; Schousboe et al., 2003; Slof Op 't Landt et al., 2008; Speakman, 2004; Xu, Long, Yang, Deng, & Deng, 2006). Heritability estimates range from 41 to 85 %, but most studies have reported heritability estimates above 50% (for a review, see Schousboe et al., 2003). According to a review by Schousboe et al. (2003), the genetics of BMI are partly gender-specific, meaning that the genes that affect women's BMI are not the same as the genes that affect men's BMI.

BMI is positively associated with several eating disorder symptoms, and high BMI may be a risk factor for eating disorders (for a review, see Jacobi et al., 2004). The eating disorder symptoms positively associated with BMI include drive for thinness, binge eating and vomiting (Bas, Bozan,& Cigerim, 2008; Burrows & Cooper, 2002; Doyle, le-Grange, Goldschmidt, & Wilfley, 2007; Fan et al., 2010; Jacobi et al., 2004; Klump, McGue, & Iacono, 2000; Lynch, Heil, Wagner, & Havens, 2008; Neumark-Sztainer, Wall, Story, & Perry, 2003; Slof Op 't Landt et al., 2008; Stice & Whitenton, 2002). Of course, the positive association between body weight and the urge to control food intake and weight can also be non-pathologic, because considering the adverse health consequences connected to overweight the urge to control food intake might be a healthy reaction (WHO, 2011b). Also, people who are overweight are often teased, discriminated against and stigmatized (Farrow & Tarrant, 2009; Puhl & Heuer, 2010), as body ideals in industrialized societies tend to be increasingly thin (Harrison, 2003; Spitzer, Henderson, & Zivian, 1999). It is therefore understandable that people who are overweight think more about dieting and weight loss than people with normal or low body weight. However, disordered eating can affect people of any body weight or size. And as there is an association between disordered eating and BMI, it is of value to consider BMI when investigating the heritability of disordered eating. To our knowledge, however, only two previous studies on the genetic and environmental effects of disordered eating have investigated the correlation between body weight and eating attitudes and behaviors. The first one, by Klump, McGue and Iacono (2000), indicated that disordered eating and body weight were partly affected by common genes, but that the majority of the genetic factors influencing disordered eating were independent of the the genetic factors

behind BMI. However, the sample consisted of female adolescents only. The second similar study (Slof-Op 't Landt et al., 2008) also had a sample consisting of male and female adolescents (2,131 twins and 517 siblings), and it showed that disordered eating and BMI have a shared genetic background. However, the majority of the genetic effects on disordered eating were independent of the shared genetic effects. More studies are needed to assess this connection, especially in larger samples of both men and women of various ages. This will give researchers more information about how BMI and disordered eating overlap on a genetic level.

Aims and Hypotheses of the Present Study

The objective of the present study was to assess the effects of genes and environment on disordered eating and on BMI, exploring both unique and shared etiology in these two traits. Also, we wanted to explore whether the respective genetic etiologies of disordered eating and BMI were gender-specific, meaning that the disordered eating and BMI of women are affected by a different set of genes than the disordered eating and BMI of men.

Our first hypothesis was that disordered eating would be moderately to highly heritable in both men and in women. Secondly, we hypothesized that BMI would be highly heritable in both women and men, and that its heritability would be best described by gender-specific models. Our third and final hypothesis was that there would be shared genetic effects behind the individual variation in disordered eating and BMI. We chose the extended twin study as our research method including both twin pairs and non-twin siblings in the same sample. The inclusion of both groups resulted in a large sample size.

Method

Participants

The analyses in the present study were performed on a population-based sample of 8,033 (n_{women} = 5,422; n_{men} = 2,611) Finnish twins and their non-twin siblings. The participants were 18-49 years old (M_{women} = 26.0 years, SD_{women} = 5.4; M_{men} = 26.2 years, SD_{men} = 4.8). The number of twins in the sample was 5,521 (3,703 women and 1,818 men), leaving 2,512 non-twin siblings (1,723 women and 792 men). The sample included 557 complete monozygotic (MZ) female twin pairs and 161 complete MZ male twin pairs. The number of complete dizygotic (DZ) female twin pairs was 353 and the number of DZ male twin pairs was 142. The sample also included 418 complete female-male DZ twin pairs. For 159 female and 75 male twin participants it was not possible to determine zygosity.

The sample of the present study was a subset of the second data collection of the Genetics of Sex and Aggression (GSA) study, carried out by the Centre of Excellence in Behavior Genetics at Åbo Akademi University. This data collection was completed in 2006 and targeted all 18–33-year-old Finnish twins and their over 18-year-old siblings living in Finland. The participants' addresses were obtained from the Finnish population registry. They received a mail survey including questions about disordered eating and different aspects of sexual and aggressive attitudes and behaviors. For a more detailed account of the gathering of data for this project, please refer to Santtila et al. (2008). The overall response rate of the study was 45%. The response rate can be considered to represent an underestimate due to address changes resulting in some potential participants not receiving the request to participate. According to Statistics Finland (http://www.stat.fi) approximately 15% of Finns move each year. Considering that the data collection lasted over half a year, the real response rate could be estimated to approximately 50%. The response rate is also largely comparable to that of surveys including sex-related questions (Bailey, Dunne, & Martin, 2000).

Zygosity of the twins was determined using questionnaire items completed by the twins (Sarna, Kaprio, Sistonen, & Koskenvuo, 1978). Previous studies have shown that this kind of method of zygosity determination is 95% accurate when compared with blood type analyses (Eisen, Neuman, Goldberg, Rice, & True, 1989). The research plan was approved by the Ethics Committee of Åbo Akademi University.

Measures

Disordered eating. We assessed disordered eating with five items (see Table 1) from the self-report questionnaire the Eating Attitudes Test 26 (EAT-26; Garner, Olmsted, Bohr, & Garfinkel, 1982). The EAT-26 is an abbreviated 26-item version of the original 40-item Eating Attitudes Test created by Garner and Garfinkel in 1979. The EAT has been widely used as a self-report measure of symptoms generally related to eating disorders in both clinical and nonclinical environments (Mintz & O'Halloran, 2000; Nasser, 1997; Orbitello et al., 2006). The instrument has very good internal consistency, with Cronbach's α values ranging from .83 to .90 (Doninger, Enders, & Burnett, 2005; Garner et al., 1982; Joiner & Kashubeck, 1996; Koslowsky et al., 1992)

The five EAT-26-items in the present study were chosen because they assessed both anorexic and bulimic eating attitudes and behavior. Our five items measured drive for thinness, dieting, preoccupation with food, intense fear of being fat, and attempts of self-induced vomiting – all of which are symptoms of disordered eating. The four first-mentioned

items were characteristic symptoms in anorexia nervosa as well as bulimia nervosa and EDNOS. The last item recording attempts of self-induced vomiting is concordant with the symptoms of bulimia nervosa and EDNOS. The five items were translated into Finnish and included in a mail survey containing questions about several phenotypic behaviors, including aggression, sexuality, body image and alcohol use. The participants answered the questions on five-point Likert-type scales ranging from 1 (*completely disagree*) to 5 (*completely agree*), higher values indicating higher levels of disordered eating. Cronbach's α was .72 for men and .78 for women, indicating acceptable reliability.

Body Mass Index. Body Mass Index (BMI) is an index of a person's weight-to-height proportionality (World Health Organization, 2011a). It is commonly used to classify underweight and overweight in adults. BMI is defined as the weight of a person in kilograms divided by the square of the person's height in meters (i.e., BMI = [kg] / $[m]^2$). The normality range of BMI is between the minimum of 18.50 and the maximum of 24.99 (World Health Organization, 2011a). The mean BMI in our sample was 23.01 (Range 14.03-61.35; *SD* = 4.09) for women and 24.55 (Range 16.51-37.09; *SD* = 3.56) for men.

Analyses

Descriptive analyses. We used SPSS for Windows version 17.0 (SPSS Inc., 2008) to compute the following phenotypic analyses. First, we explored the proportions of positive answers (i.e., *somewhat agree* or *completely agree*) and negative answers (i.e., *somewhat disagree* or *completely disagree*) for each item. This was done separately for men and for women. We also computed analyses of gender differences in each of the five disordered eating items and in BMI with Generalized Estimated Equations (GEE) to control for dependence between family members. Then, we used Pearson's *r* product-moment correlations to analyze the disordered eating data. Correlations were computed separately for men and women between all disordered eating variables, BMI, and age.

Factor analyses. In order to test the possibility of compressing the disordered eating data into a single composite variable, we tested the dimensionality of the data with a factor analysis. Our assumption was that the data would be uni-dimensional and could be compressed. We computed factor analyses for the whole sample and then men and women separately in order to explore whether the disordered eating instrument measured the same dimension in men as in women.

Univariate model fitting analyses. All genetic analyses were conducted using the Mx statistical package for Windows (Neale, Boker, Xie, & Maes, 2003). The script was set

up to include all twins whose zygosity had been successfully determined, and up to six additional siblings per family. If more than three male or more than three female siblings per family had returned the survey, those siblings that were closest in age to the twin pair were selected for the analyses.

First, intragroup correlations on disordered eating and BMI were computed in order to screen for genetic and environmental effects on phenotypic variation. Genetic and environmental influences can be separated in the twin design because genetic resemblance varies as a function of zygosity, whereas familial resemblance caused by shared environmental influences is assumed not to. Specifically, MZ twins are genetically identical, whereas DZ twins and non-twin siblings share on average 50% of their genes. In contrast, environmental influences that contribute to familial resemblance are assumed to affect MZ and DZ twins equally (Plomin et al., 2001). This means that if MZ correlations are remarkably higher than DZ correlations, a genetic influence on the disordered eating phenotype can be assumed and further explored.

Second, we assessed the potential sources of individual variations in the disordered eating and BMI phenotypes, using a twin modeling approach (Kendler, 1993). This model is based on the understanding that the observed (phenotypic) variance (*Vp*) in a trait is a linear function of additive genetic effects (*A*), non-additive genetic effects (*D*), shared environmental effects (*C*), and unique environmental effects (*E*) (i.e., $Vp = A + D + C + E$). Additive genetic influence refers to the total effects of multiple alleles on the phenotype. Non-additive genetic influence refers to the interactive effect among multiple alleles (i.e., dominance). Shared and unique environmental influences refer to non-genetic influences that contribute to familial resemblance among relatives and non-genetic influences that uniquely influence individuals, respectively. When estimating these components, measurement error was subsumed under the unique environmental source of variance. A twin model that includes additive genetic influences, non-additive genetic influences, shared and unique environmental influences simultaneously would not be statistically identified. In a twin sample, either a model with additive genetic influences, shared and unique environmental influences (an '*ACE*' model) or a model with additive genetic influences, non-additive genetic influences, and unique environmental influences (an '*ADE*' model) is estimated, depending on the twin correlations. When DZ correlations were less than one half of the MZ correlations, both *ADE* and *ACE* models were estimated for comparative purposes (Martin et al., 1978).

Disordered eating and BMI were both analyzed with univariate model-fitting scripts using maximum likelihood analysis. Men and women were analyzed separately to allow for the possibility that different genetic mechanisms could be active in the disordered eating of men and women. The fit of the different models was compared by taking the fit function (-2×log-likelihood of data) and the degrees of freedom of the *ACE* (or *ADE*) model and subtracting it from the fit function and degrees of freedom of the *AE*, *CE* (or *DE*), and *E* models. The subtraction gives a χ^2-value and associated degrees of freedom, which can be tested for significance. Between models with equal fit according to the χ^2- test, the Akaike Information Criterion (*AIC*) was used as an additional index of model fit (Akaike, 1987). Models having lower *AIC* values are preferred.

Analyses of gender differences. Tests of quantitative and qualitative gender differences in the genetics of disordered eating and BMI were computed in order to explore whether the genetics of disordered eating and BMI differed depending on a person's gender. When testing for quantitative gender differences, the fit of a reduced *ACE* (or *ADE*) model, where the estimates of *A*, *C* (or *D*), and *E* are equated for men and women, is compared to the fit of a full *ACE* (or *ADE*) model where *A*, *C* (or *D*), and *E* are estimated freely for men and women.

Qualitative gender differences were also tested. The term qualitative genetic gender differences refers to differences in the genes affecting the phenotype in question. In order to investigate if different additive genetic factors were active in disordered for men and for women, the genetic correlations between male-female DZ twins on disordered eating and on BMI are set at 0.5. The fit of this model was compared to the fit of a full model where the genetic correlation for male-female DZ twins is estimated freely.

Bivariate model fitting analyses. We assessed the possibility of disordered eating and BMI having shared genetic backgrounds with a bivariate model fitting analysis. The basis of multivariate genetic analyses lies in the exploring of cross-covariance in relatives. By comparing MZ and DZ cross-twin cross-trait correlations (e.g., disordered eating score of Twin 1 with the BMI of Twin 2), conclusions can be made regarding whether the same genetic or environmental factors influence different phenotypes. If MZ cross-twin cross-trait correlations in genetic effects are higher than the respective DZ correlations, genetic effects influencing the traits are at least partly shared. Model fit was estimated with the same χ^2 goodness-of-fit statistic mentioned above, using *AIC* as an additional fit statistic.

Results

Descriptive Results

Women were more prone to agree or somewhat agree on all five questions on disordered eating (see Table 1). The largest gender difference in proportion of positive answers was found on the item measuring attempts to vomit after meals. When asked if they had ever tried to vomit after having eaten, 10.6% of the women and 1.1% of the men agreed or somewhat agreed. The smallest gender difference was found in the proportion of participants trying to diet. Here, 31.0 % of males and 56.0 % of females agreed or somewhat agreed when asked if they tried to diet.

Table 1

Disordered Eating Displayed by Participants (in %) in a Population-based Sample of Finnish Twins and Their Siblings

	Women		Men	
	Agree or somewhat agree	Disagree or somewhat disagree	Agree or somewhat agree	Disagree or somewhat disagree
Intense fear of being fat	43.7	45.9	17.5	74.5
Preoccupation with food	27.0	61.3	9.5	81.1
Self-induced vomiting	10.6	85.6	1.1	97.6
Dieting	57.6	34.9	31.0	63.3
Drive for thinness	34.5	59.0	9.1	86.3

Note. The sample consisted of 8033 Finnish twins and their siblings aged 18-49, of which 5422 were women and 5411 were men. Disordered eating was measured with 5 items from the Eating Attitudes Test (EAT-26; Garner et al., 1982). The participants answered the questions on five-point Likert-type scales ranging from 1 (*completely disagree*) to 5 (*completely agree*), higher values indicating higher levels of disordered eating. The proportion of participants who completely agreed or somewhat agreed were compressed into the category *Agree or somewhat agree*, whereas the proportion of participants who completely disagreed of somewhat disagreed were compressed into the category *Disagree of somewhat disagree*. The participants who answered *Can not say* were not included in either group.

Wald's χ^2-test of gender differences indicated that the mean levels for all items measuring disordered eating were significantly higher in women than in men men (see Table 2). Gender differences in BMI were also tested with Wald's χ^2, and the results indicated significant differences is men's and women's mean BMI (see Table 2).

All five disordered eating items were positively associated with one another, with significant Pearson's *r*-intercorrelations ranging from .13 to .62 (see Table 2). Disordered eating and BMI also had significant positive correlations. In other words, the higher BMI a person had, the more she or he was likely to think about dieting and compensating for food intake.

Factor Analyses

A factor analysis for testing the possibility of compressing the disordered eating data into a single composite variable was first computed for the whole group. Factorability was assessed with the Kaiser-Meyer-Olkin measure of sampling adequacy (*KMO*), which measures the strength of the relationship among the variables. The *KMO* measure of .81, together with Bartlett's test of sphericity being significant ($p < .001$), indicated that the degree of common variance among the five variables was good, and that a factor model was appropriate. All anti-image correlation matrix diagonal values were also > .70, further indicating good factorability. The factor analysis yielded one factor with an eigenvalue exceeding 1 (Eigenvalues 2.78 for the first factor and < .90 for the rest). This first factor contained 55.6% of the variance. As these measures showed good factorability, a composite variable measuring disordered eating behaviors and attitudes was thus calculated from the items. To check for possible gender differences in dimensionality, we also conducted separate factor analyses for the male participants (*KMO* = .77, Bartlett's Test of Sphericity $p < .001$, all anti-image correlation matrix diagonal values > .70) and the female participants (*KMO* = .81, Bartlett's Test of Sphericity $p < .001$, all anti-image correlation matrix diagonal values > .70) respectively. Both yielded equally strong one-factor solutions (men: Eigenvalues 2.41 for the first factor explaining 48.2 % of the variance and < 1.0 for the rest; women: Eigenvalues 2.70 for the first factor explaining 53.9% of the variance and < .90 for the rest).

Table 2

Pearson's r Intercorrelations, Means, Standard Deviations and χ^2-values for Disordered Eating, Body Mass Index (BMI) and Age in a Finnish Population-based Sample (n = 8,033) of Twins and Their Siblings.

	Age	BMI	Intense fear of being fat	Preoccupation with food	Self-induced vomiting	Dieting	Drive for thinness	Disordered eating	*Mean*	*SD*
Age		.17**	-.10**	-.05**	-.10**	.02	-.06**	-.07**	25.98	5.36
BMI	.27**		.20**	.21**	0.02	.46**	.33**	.35**	23.01	4.09
Intense fear of being fat	.04*	.24**		.51**	.27**	.52**	.59**	.79**	2.88	1.42
Preoccupation with food	.02	.23**	.37**		.31**	.45**	.53**	.76**	2.33	1.38
Self-induced vomiting	-.01	.06**	.15**	.13**		.21**	.27**	.51**	1.46	1.12
Dieting	.16**	.54**	.44**	.31**	.13**		.62**	.78**	3.22	1.50
Drive for thinness	.06**	.38**	.51**	.41**	.20**	.55**		.83**	2.48	1.43
Disordered eating	.10**	.47**	.76**	.65**	.31**	.79**	.80**		2.48	1.03
Mean	26.23	24.55	2.00	1.70	1.07	2.25	1.52	1.71		
SD	4.80	3.56	1.16	1.02	.42	1.40	.98	.72		
Test of gender differences (Wald χ^2)		255.27	798.08	494.57	463.32	729.69	1,171.81			

Note. Values for women are presented above the diagonal and values for men are presented below the diagonal. BMI = Body Mass Index = kg/m². Disordered eating was assessed with five items from the Eating Attitudes Test (EAT26; Garner & Garfinkel, 1982): Intense fear of fat, Preoccupation with food, Self-induced vomiting, Dieting, and Drive for thinness. Each item was measured on a five-point self-evaluation scale ranging from *1 = Completely disagree* to *5 = Completely agree*. Disordered eating = Composite variable for the five EAT-items.

***. $p < .0001$ (2-tailed)

**. $p < .001$ (2-tailed)

*. $p. < .01$ (2-tailed)

As the factor solutions were similar for men and for women, a composite score based on the factor analysis with both genders was adequate. This composite score variable was created for each participant by adding the points of all his or her responses on the disordered eating questions together and dividing the sum by the number of valid responses given by that participant.

Gender differences in disordered eating composite scores were tested, showing a significant difference similar to the one in the five original items (see Table 2). Gender-specific bivariate correlations computed for disordered eating, BMI, and age were all statistically significant, showing the same tendencies as for the individual items. This means that disordered eating was positively associated with BMI in both men and women, and that the positive association between age and disordered eating in men and the negative association between age and disordered eating in women remained significant.

Univariate Model Fitting Results

Twin intraclass correlations of disordered eating suggested that the phenotype varied as a function of twin zygosity, and we could therefore assume that genetic influences affected both phenotypes. The correlations were .65 for male MZ –pairs and .35 for male DZ pairs, .54 for female MZ pairs and .18 for female DZ pairs, and -.05 for female-male DZ pairs (see Table 3 for confidence intervals). The twin intraclass correlations for BMI were .79 for male MZ pairs, .49 for male DZ pairs, .81 for female MZ pairs, .35 for female DZ pairs, and .10 for female-male DZ pairs (see Table 3 for confidence intervals). Since twin intraclass correlations for female MZ pairs were more than double the size of the DZ correlations for both disordered eating and for BMI, (see Table 3), we concluded that non-additive effects (*D*-effects) were a possible factor in the development of both phenotypes. Therefore, both *ACE*-(additive genetic effects + shared environmental effects + unique environmental effects) and *ADE*-models (additive genetic effects + non-additive genetic effects + unique environmental effects) were fitted to the data.

Table 3

Twin Intraclass Correlations and Confidence Intervals for Disordered Eating and Body Mass Index in a Population-based Sample of Finnish Twin Pairs.

	Disordered eating		Body Mass Index	
	r	95 % *C.I.*	*r*	95 % *C.I.*
Monozygotic male twin pairs	.65	.54 – .73	.79	.72 – .83
Dizygotic male twin pairs	.35	.04 – .54	.49	.30 – .62
Monozygotic female twin pairs	.54	.48 – .59	.81	.79 – .84
Dizygotic female twin pairs	.18	.07 – .28	.35	.23 –.44
Dizygotic female-male twin pairs	-.05	-.13 – .04	.10	-.01 – .21

Note. Disordered eating was measured with a composite variable consisting of five items from the Eating Attitudes Test (Garner et al., 1982). Body Mass Index is a measure of a person's weight-to-height proportionality, defined as the weight of a person in kilograms divided by the square of the person's height in meters (i.e., BMI = [kg] / $[m]^2$). *C.I.* = Confidence intervals on a 95 % significance level.

When testing the *ACE*-model for disordered eating, we found that the shared environment component (*C*) could be dropped without any significant decrease in model fit, thus making an *AE*-model the best fit. This was the case for both women and men. The *ADE*-model fitting for disordered eating led to very similar results, indicating that the non-additive effects (*D*) component could be dropped for both genders, without the fit measures decreasing significantly. Therefore, the model of best fit was an *AE*-model in this case as well. In this model, additive genetic effects accounted for 50% of disordered eating in women and 62% of disordered eating in men, with unique environmental effects explaining remaining variance. All parameter estimates and fit statistics of the univariate model fitting for disordered eating are presented in Table 4.

Table 4

Univariate Model Fitting Results for Disordered Eating in a Population-Based Sample of Finnish Twins and Their Siblings

Model	Compared with model	*A*	*C/D*	*E*	*-2LL*	*AIC*	$\Delta\chi^2$	Δdf	*p*-value
Women									
1. *ACE*		0.50	0.00	0.50	18531.27	4955.273			
2. *AE*	**1**	**0.50**	**-**	**0.50**	**18531.27**	**4953.273**	**0.000**	**1**	**1.000**
3. *CE*	1	-	0.28	0.72	18592.35	5014.353	61.080	1	<.001
1. *ADE*		0.50	0.00	0.50	18532.578	4956.578			
2. *AE*	**1**	**0.50**	**-**	**0.50**	18532.578	4954.578	**0.000**	**1**	**0.999**
3. *DE*	1	-	1.00	0.00	18595.047	5017.047	62.469	1	<.001
Men									
1. *ACE*		0.62	0.00	0.38	18531.27	4955.273			
2. *AE*	**1**	**0.62**	**-**	**0.38**	**18552.70**	**4974.702**	**0.000**	**1**	**1.000**
3. *CE*	1	-	0.35	0.65	18552.70	4974.702	21.429	1	<.001
1. *ADE*		0.62	0.00	0.38	18532.578	4956.578			
2. *AE*	**1**	**0.62**	**-**	**0.38**	18532.578	4954.578	**0.000**	**1**	**0.999**
3. *DE*	1	-	1.00	0.00	18557.145	4979.145	24.566	1	<.001

Note. Disordered eating was measured with a composite variable consisting of five items from the Eating Attitudes Test (Garner et al., 1982). The model with best model fit is indicated in bold. *A* = additive genetic effects; *C* = shared environmental effects; *D* = non-additive genetic effects; *E* = unique environmental effects; *AIC* = Akaike Information Criterion; *-2LL* = -2xlog likelihood of data; *df* = degrees of freedom.

The heritability of BMI was also tested with both *ACE*- and *ADE*-models. When testing the *ACE*-model for BMI, we found that the *C* component could be dropped without any significant decrease in model fit, thus making an *AE*-model the best fit. This was the case for both women and men. The *ADE*-model fitting for disordered eating led to very similar results, indicating that the non-additive effects (*D*) component could be dropped for both genders, without the fit measures decreasing significantly. Therefore, the model of best fit was an *AE*-model in this case as well. When testing the *ACE*-model, additive genetic effects accounted for 80% of BMI in women and 78% of BMI in men, with unique environmental effects explaining remaining variance. The *ADE*-model fitting yielded *A*-estimates of 80% for

women and 77% for men, with *E*-effects accounting for the rest of the variance. All parameter estimates and fit statistics of the univariate model fitting for BMI are presented in Table 5.

Table 5

Univariate Model Fitting Results for Body Mass Index in a Population-Based Sample of Finnish Twins and Their Siblings

Model	Compared with model	*A*	*C/D*	*E*	*-2LL*	*AIC*	$\Delta\chi^2$	Δdf	*p*-value
Women									
1.*ACE*		0.80	0.00	0.20	35615.855	22555.855			
2.*AE*	**1**	**0.80**	**-**	**0.20**	**35615.86**	**22553.855**	**0.000**	**1**	**1.000**
3.*CE*	1	-	0.40	0.60	35847.841	22785.841	231.985	1	<.001
1.*ADE*		0.80	0.00	0.20	35609.539	22549.539			
2.*AE*	**1**	**0.80**	**-**	**0.20**	**35609.539**	**22547.539**	**0.000**	**1**	**0.993**
3.*DE*	1	-	1.00	0.00	35922.015	22860.015	312.476	1	<.001
Men									
1.*ACE*		0.73	0.04	0.22	35615.855	22555.855			
2.*AE*	**1**	**0.78**	**-**	**0.22**	**35616.196**	**22554.196**	**0.341**	**1**	**0.559**
3.*CE*	1	-	0.45	0.55	35681.392	22619.392	65.537	1	<.001
1.*ADE*		0.77	0.00	0.23	35609.539	22549.539			
2.*AE*	**1**	**0.77**	**-**	**0.23**	**35609.539**	**22547.539**	**0.000**	**1**	**0.998**
3.*DE*	1	-	1.00	0.00	35725.268	22663.268	115.728	1	<.001

Note. Body Mass Index is a measure of a person's weight-to-height proportionality, defined as the weight of a person in kilograms divided by the square of the person's height in meters (i.e., BMI = [kg] / $[m]^2$). The model with best model fit is indicated in bold. *A* = additive genetic effects; *C* = shared environmental effects; *D* = non-additive genetic effects; *E* = unique environmental effects; *AIC* = Akaike Information Criterion; *-2LL* = -2xlog likelihood of data; *df* = degrees of freedom.

Tests of Gender Differences

The *AE*-model for disordered eating where the *A*- and *E*-components were allowed to vary between men and for women had a -2×times log-likelihood of data (*-2LL*) of 18,531.27 and an Akaike's Information Criterion (*AIC*) of 4,951.27. Testing for quantitative genetic gender differences showed that model fit did not deteriorate when constricting the genetic estimates to be equal between men and women (*-2LL* = 18,532.88, *AIC* = 4,950.88, $\Delta\chi^2$ = 1.61, $\Delta df = 1$, $p = .21$). This means that there was no significant gender difference in the degree to which disordered eating is heritable. However, when testing qualitative gender differences in the genetics of disordered eating, we found a significant impairment of model fit (*-2LL* = 18,583.40, *AIC* = 5,001.40, $\Delta\chi^2 = 50.82$, $\Delta df = 1$, $p < .001$). This means that the genes that contribute to disordered eating in women were only partly the same that those contributing to disordered eating in men.

BMI was also tested for quantitative and qualitative gender differences. The *AE*-model for BMI where the *A*- and *E*-components were allowed to vary between men and for women had a *2LL* value of 35,616.20 and an *AIC* of 22,552.20. Here, both quantitative (*-2LL* = 35,633.22, *AIC*=22,567.22, $\Delta\chi^2 = 17.02$, $\Delta df = 1$, $p < .001$) and qualitative (*-2LL* = 35,672.20, *AIC*=22,604.20, $\Delta\chi^2 = 56.00$, $\Delta df = 2$, $p < .001$) differences in genetic effects were discovered, as model fit deteriorated both when assuming both kinds of similarity in genetic backgrounds. Consequently, genes affected women's BMI more than they do men's BMI, and the genes affecting BMI in women are partially not the same than the genes affecting BMI in men.

Bivariate Model Fitting Results

Bivariate analyses indicated partial shared heritability in BMI and disordered eating. The genetic (r_g) correlation between disordered eating and BMI was .47 for women and .69. The unique environmental (r_e) correlations were .19 for women and .17 for men. Confidence intervals are presented in Figure 1. For women, 83.2% of the phenotypic correlation was explained by shared additive genetic effects, and 16.8% of the phenotypic correlation was explained by shared unique environmental effects. For men, 87.3% of this correlation was explained by shared additive genetic effects and 12.7% was explained by shared unique environmental effects. This means that the two traits share a considerable share of their genetic bases.

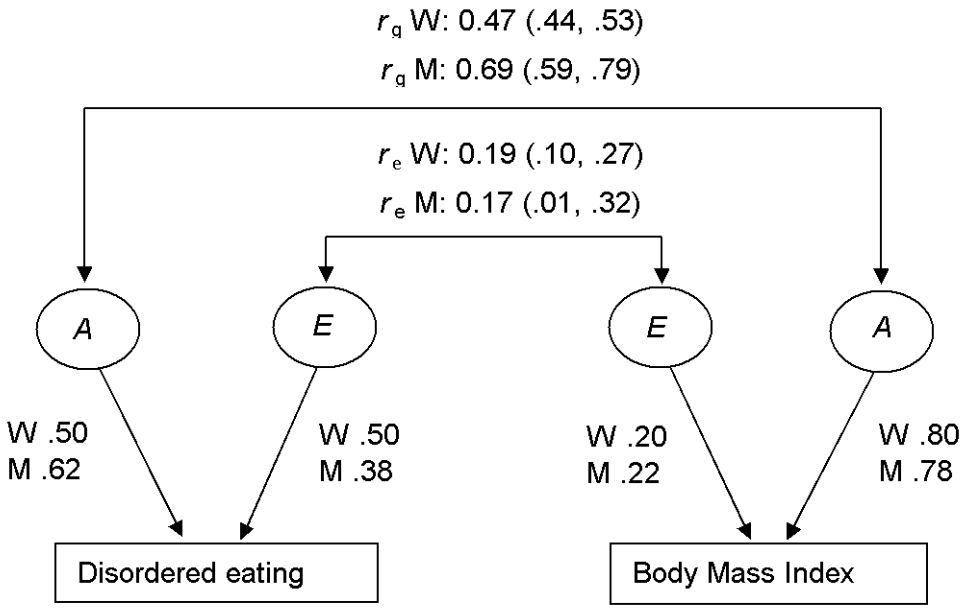

Figure 1. Bivariate model fitting results showing shared and non-shared additive genetic and unique environmental effects on disordered eating and Body Mass Index in a population-based sample of Finnish twins and their siblings. r_a = additive genetic correlation; r_e = unique environmental correlation; M = men; W = women; *A* = additive genetic effects; *E* = unique environmental effects.

Discussion

The aim of the present study was assessing the proportions of genetic and environmental effects affecting disordered eating and Body Mass Index (BMI) using an extended twin study spproach. Shared and unique etiologies in the two traits were explored for both men and women, and gender differences in genetic etiology were explored through bivariate model fitting analyses.

Phenotypic Differences and Associations

The women in our sample reported having more disordered eating than the men on all five questions assessing disordered eating. Nonetheless, unexpectedly high prevalences of disordered eating were discovered in both genders. In fact, almost two thirds of the women (57.6%) indicated that they were currently trying to diet. The proportion of men trying to diet was almost one third (31.0%). Another noteworthy result derived from answers on the individual disordered eating items was the proportion of women who reported having tried to vomit after eating. This proportion was unexpectedly large (10.6%), given that the present sample was a non-clinical population-based one, consisting of adults. In studies with adolescents and with young adults, this kind of purging is more prevalent.

The female participants had a lower mean BMI than the male participants, but the mean BMI of both women (23.01) and men (24.55) were clearly situated on the top half of the normal range of BMI (18.50-24.99). These results reflect recent trends in the average BMI of the Finnish population and of people in industrialized societies in general, as overweight in adults has become the norm rather than the exception (Speakman, 2004; World Health Organization, 2011b). In fact, the Finnish population is among the most overweight in Europe (International Association for the Study of Obesity, 2008)

The Heritability of Disordered Eating and BMI

The strong monozygotic twin associations between disordered eating and BMI as compared to dizygotic and non-twin siblings indicated genetic effects for both disordered eating and BMI. However, the complete lack of association in disordered eating in female-male DZ twin pairs was interesting and unexpected, especially as there still was a significantly positive association in disordered eating between the siblings in female-male non-twin sibling pairs. Why opposite sex twins seem to have no association in eating attitudes and behaviors and opposite sex non-twins have a positive one is uncertain, especially since no other study has yielded similar results. One hypothesis is that this result could point to an effect specific to dizygotic twins. Such an effect could obviously be either

pre- or postnatal. However, in order to establish that such effects might exist, this result would first have to be replicated by doing more extended twin studies.

Our hypothesis about disordered eating being moderately or highly heritable was supported; the heritability estimate for disordered eating in women (50%) corresponded with earlier research (Bulik, Sullivan, & Kendler, 1998; Jacobi et al., 2004; Javaras et al., 2008; Klump et al., 2009; Striegel-Moore & Bulik, 2007). The estimated heritability for men was also high (62%). More precisely, individual differences in disordered eating in both women and men were best explained by additive genetic effects and unique environmental effects, meaning that shared environmental effects could be dropped without a decrease in the fit of the explanatory model. This kind of an explanatory model has proven to be best fit in most previous studies exploring the disordered eating of women. As stated in the introduction of this study (see *Assessing the Heritability of Disordered Eating*), studies on the heritability of the disordered eating in men have yielded inconsistent results (Baker et al., 2009; Eiben, 2007 (as referred to in Baker et al., 2009); Keski-Rahkonen, Bulik, et al., 2005; Keski-Rahkonen, Neale, et al., 2005; Reichborn-Kjennerud et al., 2003; Reichborn-Kjennerud, Bulik, Kendler, et al., 2004; Reichborn-Kjennerud, Bulik, Tambs, & Harris, 2004; Slane, Burt, & Klump, 2007 (as cited by Baker et al., 2009); Slof Op 't Landt et al, 2008; Tholin, Rasmussen, Tynelius, & Karlsson, 2005), rendering comparison difficult. As summarized by Baker et al. (2009), research has until now indicated that disordered eating is less heritable in men than in women. The results of the present study yielded numerically higher heritability estimates for disordered eating in men (62 %) than in women (50 %), although tests of quantitative gender differences did not indicate significant results. Qualitative gender differences in the heritability of disordered eating were discovered, however. The discovery of qualitative genetic gender differences has implications for future research, as it implies that association and linkage studies on disordered eating will likely yield somewhat different results for men as compared to women.

Our second hypothesis was that BMI would be highly heritable. As expected, the heritability estimates of BMI were high for both men (78%) and women (80%). Additionally, the gender differences in heritability were similar to previous studies (Lajunen et al., 2009; Schousboe et al., 2003), meaning that BMI is more heritable in women than in men. Also, the genes affecting it were not completely the same in women as they are in men.

We were surprised to find that the numerically small quantitative gender differences in the heritability estimates of BMI were significant, whereas the numerically large gender

difference for estimates for disordered eating was not. This may be explainable by the the relatively precise nature of BMI as a measure, compared to the measure of disordered eating that has lower reliability.

The third and final hypothesis of the present study was that at least a moderate portion of the phenotypic variance in disordered eating was accounted for by the same genes that affect BMI. As stated in the introduction, only two studies on the shared genetics of disordered eating and BMI have been done (Klump et al., 2000; Slof Op 't Landt, 2008). These indicated moderate shared genetic effects, so we expected our analyses to yield similar results. In fact, our bivariate model fitting yielded high genetic correlations for men (r_g = .69). The genetic correlation for women was lower, but still substantial (r_g = .47). Consequently, the phenotypic association between disordered eating and BMI was primarily explained by common genetic influences in men and partially explained by common genetic influences in women. We are not sure of how our results should be interpreted, but one possibility is that high body weight might exist before the disordered eating, and that it may, together with body dissatisfaction, weight-related teasing, or other factors, lead to disordered eating attitudes and behaviors. After all, high body weight and body dissatisfaction and/or negative body image often precede disordered eating and are considered risk factors for developing disordered eating (Jacobi et al., 2004). Also, Slof Op 't Landt et al. (2008) suggested that the direction of the causation might be the inverse, so that the genetic basis of disordered eating would lead to disordered eating, which in turn would lead to weight fluctuation.

The Strengths of the Present Study

The present study is important because knowing what causes or affects disordered eating is a necessary foundation for planning treatment and prevention. Disordered eating is still often perceived as a set of behaviors primarily caused by factors in the social environment, but the increasing number of results indicating moderate to strong heritability have given reason to start emphasizing genetics as much as culture and socialization, if not even more, when talking about the why some individuals display disordered eating and others do not (DeAngelis, 2002). The results of studies such as the present one should therefore be incorporated into the information on disordered eating given to caregivers and to the people who educate caregivers, especially as emphasizing socialization-based theories instead of genetics-based theories of the etiology of disordered eating has been proven to make health care students readier to place the blame for the disorder on the patient (Crisafulli, Van Holle,

& Bulik, 2008). A similar pattern has been found in studies comparing how much caregivers blame and dislike patients with eating disorders compared to patients with psychiatric disorders that are more commonly perceived as genetic in origin. For instance, patients suffering from depression or schizophrenia were rated as more likeable and less accountable for their illnesses than patients with anorexia nervosa (Roehrig & McLean, 2010; Stewart, Keel, & Schiavo, 2006). Therefore, emphasizing the genetic etiology of disordered eating might make care providers more positive towards patients exhibiting disordered eating. This, in its turn, might lead to patients obtaining more empathic responses from caregivers, which eventually could lead to faster recovery (Halper, 2003).

Besides the importance of studying heritability of disordered eating in general, the present study's specific strengths compared to previous studies lay in its large population-based sample and its inclusion of both women and men. Also, there are very few studies on the heritability of disordered eating in non-adolescent samples. Furthermore, the inclusion of non-twin siblings and opposite-sex sibling pairs allowed for us to test genetic gender differences, which have yet to be studied thoroughly. Finally, the present study has the largest sample yet to be used in a study of the shared genetic basis disordered eating and BMI. The findings of the present study indicating shared genetic etiology in disordered eating and BMI may have implications for future association and linkage studies, that is, studies on specific genes and their impact on these phenotypes.

Limitations and Methodological Considerations

The prime limitation of the present study was that disordered eating was assessed with merely five items. The term disordered eating, as used in the present study, included trying to diet, being afraid of gaining weight, having an intense wish to be thinner, trying to vomit after meals and thinking excessively about food. It did not constitute a DSM-IV or ICD-10 defined diagnostic category, although it measured behaviors that are characteristic of the clinical eating disorder diagnoses. Therefore, the strength of the present study lays not so much in its link to specific psychiatric diagnoses as it does in its ability to make predictions on sub-clinical tendencies that are more prevalent and measured on a continuum.

The disordered eating measures of the present study assessed both cognitions and actions. Their belonging to a single genetic component can be contested, as it is not certain that cognitions linked to disordered eating always translate in the way a person actually behaves. As for example perfectionism and other personality traits have been found to be highly genetic and strongly associated to disordered eating (Bardone-Cone et al., 2007;

Forbush, Heatherton, & Keel, 2007), it is possible that what this study shows is not only the heritability of disordered eating in itself, but an underlying dimension of perfectionism or of some other moderating dimension that is strongly associated to disordered eating.

The suitability of the twin study as a method of studying disordered eating has also been contested, especially with regards to the equal environments assumption. However, Klump, Holly, Iacono, McGue, and Willson (2000) proved in a test of the equal environments assumption that physical twin similarity does not affect pairwise concordance in disordered eating.

Conclusions and Future Prospects

The heritability of disordered eating in men is still relatively unexplored, as are the gender differences in genetic effects on disordered eating. Even though the low prevalence of clinical diagnoses in men makes it hard to make powerful predictions about their heritability, men's disordered eating can be easily explored in twin populations if it is measured on a continuum rather than as a dichotomous variable, as was done in the present study.

Furthermore, the genetic association between BMI and disordered eating is of importance to study more, and might be of worth to researchers wishing to explore further how the connections between body weight and disordered eating work. Knowing that both traits are heritable and knowing that there are some etiological commonalities between them may helpful to future researchers who wish to further disentangle the etiology of disordered eating and to find how it is affected by other aspects.

In conclusion, this study explored the heritability of disordered eating and BMI, and our expectations to find genetic effects on both were confirmed. Therefore, the present study was successful in providing further evidence on that individual differences in disordered eating are determined by qualitatively gender specific moderate to strong genetic effects, and that disordered eating and BMI share a considerable share of their genetic bases.

Svensk Sammanfattning

Inledning

Ätstörningar är livshotande och allvarliga sjukdomar (Klump, Bulik, Kaye, Treasure, & Tyson, 2009) vars främsta kännetecken är betydande störningar i ätbeteenden och –attityder (American Psyhiatric Association, 2000). Sjukdomsmanualen *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association, 2000) innehåller två typer av kliniska ätstörningar. Den första, *anorexia nervosa*, kännetecknas av att en person avsiktligt håller sin vikt mycket låg. Den andra, *bulimia nervosa*, kännetecknas av episoder av hetsätning med påföljande rensning. Rensningen kan till exempel innebära uppkastning efter hetsätningen. De ätstörningar som inte passar in på kriterier för någondera får diagnosen *Eating Disorder Not Otherwise Specified* (EDNOS).

Stört ätbeteende har en multifaktoriell etiologi, vilket betyder att flera komponenter påverkar hur stört ätbeteende utvecklas. Genetiska, biologiska och temperamentsmässiga variationer interagerar med miljömässiga faktorer och resulterar tillsammans i de individuella variationerna i fenotypen stört ätbeteende (Klump et al., 2009). Ett sätt att avgöra omfånget av genernas respektive omgivningens inverkan på ett beteende är att bedriva tvillingstudier. Enligt tvillingstudier beräknas de genetiska effekterna bakom anorexia nervosa, bulimia nervosa och EDNOS variera mellan 28 % och 88 % (Bulik, Sullivan, & Kendler, 1998; Jacobi et al., 2004; Javaras et al., 2008; Klump et al., 2009; Striegel-Moore & Bulik, 2007).

Trots att det finns mycket forskning kring ärtftligheten av stört ätbeteende består samplen nästan uteslutande av kvinnor. De få resultat som finns om stört ätbeteende hos män är motstridiga (se t.ex. Javaras et al., 2008; Keski-Rahkonen et al., 2005; Reichborn-Kjennerudd, Bulik, Tambs, & Harris, 2004; Schur, Noonan, Polivy, Goldberg, & Buchwald, 2009; Slof Op 't Landt et al, 2008). Också forskning över huruvida de genetiska riskfaktorerna är lika för män och kvinnor har kommit fram till motstridiga resultat.

Body Mass Index (BMI) är ett mått på hur er persons kroppsvikt förhåller sig till hennes eller hans längd. BMI är ett vida använt instrument i kliniskt arbete och i forskning, och det används främst för att definiera under- respektive övervikt (World Health Organization, 2011a). Kvinnor har oftast lägre BMI än män såväl hos finländare (Helakorpi, Paavola, Prättälä, & Uutela, 2009; Korkeila, Kaprio, Rissanen, & Koskenvuo, 1995) som i andra populationer (Schousboe et al, 2003). Det är typiskt att BMI ökar med åldern (Korkeila et al., 1995). BMI är även ärftligt i hög grad (Klump, McGue, & Iacono, 2000; Lajunen et al., 2009; Mustelin, Silventoinen, Pietiläinen, Rissanen, & Kaprio, 2009; Ortega-Alonso, Sipilä,

Kujala, Kaprio, & Rantanen, 2009; Schousboe et al., 2003; Slof Op 't Landt et al., 2007; Speakman, 2004; Xu, Long, Yang, Deng, & Deng, 2006). Ärftlighetestimaten varierar mellan 41 % och 85 %, och en absolut majoritet av estimaten ligger på över 50 % (Schousboe et al., 2003). Enligt Schousboe et al. (2003) är de gener som påverkar BMI delvis könsspecifika.

Stört ätbeteende och BMI har en stark koppling. Ju högre BMI en person har desto större är sannolikheten att hon eller han uppvisar stört ätbeteende (Jacobi et al., 2004). Att personer med högre BMI uppvisar en större vilja att kontrollera sin vikt kan förstås bero på att kroppsidealet i industrialiserade samhällen är väldigt smalt (Harrison, 2003; Spitzer, Henderson, & Zivian, 1999). Övervikt är också kopplat till flera somatiska sjukdomar (WHO, 2011b) och till diskriminering och mobbning (Farrow & Tarrant, 2009; Puhl & Heuer, 2009), alltså är det logiskt att tänka att hög BMI kan leda till stört ätbeteende. Kopplingen kan dock också vara genetisk, dvs. att BMI och stört ätbeteende påverkas av samma uppsättning gener. De två studier som hittills undersökt den genetiska kopplingen mellan BMI och stört ätbeteende lät förstå att det finns en genetisk koppling dem emellan (Klump, McGue, & Iacono, 2000; Slof-Op 't Landt et al., 2008). Samplen i dessa bestod dock enbart av ungdomar, och i en av studierna var alla deltagare kvinnor (Klump, McGue, & Iacono, 2000). Det finns alltså behov av vidare utredningar gällande den möjliga genetiska kopplingen mellan BMI och stört ätbeteende.

Syftet med föreliggande studie var att undersöka effekten av gener respektive omgivning på stört ätbeteende och BMI. Målet var också att undersöka ifall det fanns en gemensam genetisk bas för dem. Ett annat syfte var att utreda ifall den genetiska etiologin var könsspecifik, och ifall eventuella könsskillnader i de genetiska effekterna var kvalitativa eller kvantitativa. Utgående från tidigare forskningsresultat ställdes som första hypotes att stört ätbeteende är i måttlig eller hög grad ärftligt hos såväl kvinnor som män. Den andra hypotesen var att BMI skulle vara i hög grad ärftligt, och att ärftligheten av BMI skulle vara åtminstone kvalitativt könsspecifik. Den tredje och sista hypotesen var att det skulle finnas gemensamma genetiska effekter bakom stört ätbeteende och BMI.

Metod

Analyserna i den här studien gjordes på ett populationsbaserat sampel på 8 033 (n_{kvinnor} = 5 422; $n_{\text{män}}$ = 2 611) finländska tvillingar och deras syskon i åldrarna 18-49 (M_{kvinnor} = 26,0 år, SD_{kvinnor} = 5,4; $M_{\text{män}}$ = 26,2 år, $SD_{\text{män}}$ = 4,8). Av deltagarna var 5 521 (3 703 kvinnor och 1 818 män) tvillingar och 2 512 inte tvillingar (1 723 kvinnor och 792 män). Samplet hörde till ett forskningsprojekt vid Åbo Akademi vars syfte var att utreda genetiska faktorer

bakom bl.a. sexualitet och aggression. Datainsamlingen genomfördes 2006, och den riktade sig till 18–33 år gamla finländska tvillingar och deras minst 18 år gamla syskon som var bosatta i Finland. Undersökningen utfördes med frågeformulär som postades till alla deltagare. Svarsprocenten var 45 %. Tvillingarnas zygositet (dvs. huruvida de var en- eller tvääggstvillingar) avgjordes med frågor som tvillingarna svarade på (Sarna, Kaprio, Sistonen, & Koskenvuo, 1978). Eisen, Neuman, Goldberg, Rice och True (1989) har bevisat att det här frågeformuläret kan bestämma tvillingars zygositet med 95 procents säkerhet.

Vi mätte stört ätbeteende med fem frågor från självrapporteringstestet Eating Attitudes Test 26 (EAT-26; Garner, Olmsted, Bohr, & Garfinkel, 1982). Frågorna valdes ut för att de mätte såväl anorektiska som bulimiska tankar och beteenden. EAT är vida använt i kliniska sammanhang och i forskning (Mintz & O'Halloran, 2000; Nasser, 1997; Orbitello et al., 2006). Instrumentet har mycket god intern konsistens, med ett Cronbachs alpha (α) på ,83 till ,90 (Doninger, Enders, & Burnett, 2005; Garner et al., 1982; Joiner & Kashubeck, 1996; Koslowsky et al., 1992). Frågorna som användes i vår studie besvarades på en femgradig Likert-skala från 1 (*helt av annan åsikt*) till 5 (*helt av samma åsikt*). Cronbach's α var ,72 för män och ,78 för kvinnor, vilket tydde på god intern konsistens mellan variablerna.

Förutom stört ätbeteende mätte vi Body Mass Index (BMI) för deltagarna. Indexet räknas ut genom att dividera vikten i kilogram med kvadraten av längden i meter (dvs. BMI = [kg] / $[m]^2$). Normalviktsintervallet ligger mellan 18,50 och 24,99 (World Health Organization, 2011a). I vårt sampel var BMI i medeltal 23,01 (Variationsområde: 14,03–61,35; *SD* = 4,09) för kvinnor och 24,55 (Variationsområde: 16,51–37,09; *SD* = 3,56) för män.

Vi analyserade först medelvärden och könsskillnader i BMI och stört ätbeteende, och sedan utförde vi en faktoranalys för att komprimera de fem frågorna om stört ätbeteende till en summavariabel. Sedan räknade vi ut korrelationer på stört ätbeteende och BMI mellan olika typer av syskonpar. Det här gjordes för att söka efter genetiska effekter på fenotypisk variation. Genetiska och omgivningsrelaterade effekter kan separeras i tvillingstudier eftersom genetisk likhet tvillingar emellan varierar beroende av tvillingarnas zygositet, medan familjemässiga faktorer inte antas variera på samma sätt mellan tvillingar som vuxit upp tillsammans. Enäggstvillingar är genetiskt identiska, medan tvääggstvillingar delar cirka 50 % av sina gener. Omgivningseffekter som beror på familjemiljö antas påverka enäggs- och tvääggstvillingar lika mycket (Plomin et al., 2001), vilket leder till att om stört ätbeteende

har ett starkare samband mellan enäggstvillingar än mellan tvääggstvillingar kan genetiska effekter på stört ätbeteende antas och utredas vidare.

Härnäst utredde vi källan till individuell variation i stört ätbeteende och BMI genom att använda en univariat modellanalys (Kendler, 1993). Enligt den här teoretiska modellen är den observerade (fenotypiska) variationen (*Vp*) i ett drag en lineär funktion av additiva genetiska effekter (*A*), icke-additiva effekter (*D*), delade omgivningseffekter (*C*) och unika omgivningseffekter (*E*) (dvs. $Vp = A + D + C + E$). Med additiva genetiska effekter avses den totala effekten ett flertal alleler kan ha på en fenotyp. Begreppet icke-additiva effekter syftar på interaktiva effekter mellan flera alleler (dvs. dominanseffekter). Delade och unika omgivningseffekter står för icke-genetiska faktorer som ökar respektive minskar den fenotypiska likheten mellan familjemedlemmar. Såväl additiva som icke-additiva effekter kan logiskt sett inte existera i samma modell, utan i tvillingsstudier antas individuell variation antingen förklaras av en *ACE*-modell ($A + C + E$) eller en *ADE*-modell ($A + D + E$), beroende på om tvääggstvillingkorrelationerna är under eller över hälften av enäggstvilling-korrelationerna. När tvääggstvillingkorrelationerna är mindre än hälften av enäggstvillingkorrelationerna finns det skäl att testa båda modellerna på materialet (Martin et al., 1978). Univariata modellanalyser gjordes för såväl stört ätbeteende som BMI. Kvinnors och mäns data analyserades var för sig, vilket tillät oss att undersöka ifall den genetiska etiologin var könsspecifik.

Sedan undersökte vi kvantitativa och kvalitativa könsskillnader i data. Kvantitativa genetiska könsskillnader innebär könsskillnader i graden av ärftlighet, medan kvalitativa genetiska könsskillnader avser könsskillnader i vilka gener som påverkar stört ätbeteende respektive BMI.

Till sist undersökte den gemensamma genetiska etiologin i stört ätbeteende och BMI genom en bivariat modellanalys. I bivariata modellanalyser undersöker man likheten mellan familjemedlemmar genom att analysera hur en egenskap hos egenskap i familjen hänger ihop med en annan genom att räkna ut associationer i olika egenskaper mellan familjemedlemmar.

Resultat

Kvinnorna i vårt sampel uppvisade signifikant mer stört ätbeteende än männen. Stört ätbeteende och BMI var positivt korrelerade, vilket betydde att personer med proportionellt större kroppsvikt uppvisade starkare tecken på stört ätbeteende. Enligt den faktoranalys vi utförde kunde de fem frågorna om stört ätbeteende komprimeras till en summavariabel som sedan användes i de univariata och de bivariata modellanalyserna.

Eftersom korrelationen i såväl stört ätbeteende som BMI enäggstvillingar emellan var märkbart högre än tvääggstvillingar emellan kunde vi anta att stört ätbeteende och BMI är delvis ärftliga. Våra resultat från de univariata tvillingsanalyserna visade att stört ätbeteende hos kvinnor påverkades till 50 % av additiva genetiska effekter och till 50 % av unika omgivningseffekter. Hos män var motsvarande estimat 62 % och 38 %. BMI hade en starkare genetisk bas, med estimat på 80 % additiva genetiska effekter för kvinnor och 78 % additiva genetiska effekter för män. Unika omgivningseffekter stod för 20 % för variationen i BMI hos kvinnor och för 22 % av variationen hos män.

Vi hittade inga signifikanta kvantitativa könsskillnader i ärftligheten av stört ätbeteende, även om värdena för män och kvinnor varierade. Däremot fanns kvalitativa skillnader, vilket tydde på att de genetiska faktorerna bakom stört ätbeteende var delvis könsspecifika. För BMI hittades såväl kvantitativa som kvalitativa könsskillnader, vilket tydde på att BMI är mer ärftligt för kvinnor än det är för män, och att generna som påverkar BMI är delvis andra för kvinnor än för män.

De bivariata modellanalyserna tydde på att BMI och stört ätbeteende delvis påverkas av samma gener. Den genetiska korrelationen mellan stört ätbeteende och BMI var ,47 för kvinnor och ,69 för män. Korrelationen i unika omgivningseffekter var ,19 för kvinnor och ,17 för män. Hos kvinnorna i samplet berodde 83,2 % av den genetiska korrelationen på delade additiva genetiska effekter, medan 16,8 % av den fenotypiska korrelationen kunde förklaras av delade unika omgivningseffekter. För männen i vår studie var motsvarande procentandelar 87,3 % respektive 12,7 %. Med andra ord verkade det som om långt över hälften av korrelationen i BMI och stört ätbeteende orsakas av delad genetisk bakgrund i dessa.

Diskussion

Kvinnorna uppgav sig ha mera stört ätbeteende än männen gjorde, vilket är i enlighet med tidigare forskning (se inledning för referenser). Kvinnor hade i medeltal lägre BMI än män, och BMI tycktes öka med åldern. Stört ätbeteende och BMI hade en positiv korrelation, vilket betyder att ju större övervikt en person har, desto mer uppger hon eller han beteenden och tankar som är förknippade med stört ätbeteende.

I enlighet med den första hypotesen konstaterades att stört ätbeteende är i hög grad ärftligt såväl hos kvinnor som hos män. Därmed var resultaten gällande kvinnor i stort sett i enlighet med tidigare forskning med sampel som bestod av kvinnor. Resultatet för stört ätbeteende hos män stämde i stort överens med de resultat Baker et al. (2009) fick som

pekade på ärftlighet. BMI visade sig vara ärftligt i högre grad än stört ätbeteende, vilket stämmer överens med tidigare forskning. Könsskillnaderna i ärftligheten av BMI liknade också resultaten från tidigare forskning.

Den tredje hypotesen handlade om huruvida stört ätbeteende och BMI kunde delvis påverkas av samma gener. Endast två studier (Klump et al., 2000; Slof Op 't Landt et al., 2008) som studerat den här kopplingen hittades. De här studiernas resultat indikerade delade genetiska effekter, så vi förväntningen var också att hitta åtminstone en moderat koppling. De facto visade våra resultat på hög genetisk korrelation för män och medelhög för kvinnor. Dessutom visade resultaten på att över 80 % av den fenotypiska associationen mellan stört ätbeteende och BMI kan antas bero på delade genetiska effekter. Hur den här kopplingen ser ut i ett individuellt perspektiv är näst intill omöjligt att säga på basis av den här studien. Men eftersom BMI har en högre ärftlighet än stört ätbeteende kan högt BMI tänkas vara en riskfaktor som kan fungera som katalysator för stört ätbeteende. Med andra ord kunde högt BMI tänkas vara en av de egenskaper som leder till stört ätbeteende hos en individ, särskilt då någon typ av omgivningsmässig stress fungerar som katalysator för denna. Slof Op 't Landt et al. (2008) har även hävdat att det kausala sambandet även kunde vara det motsatta, så att genetiskt betingat stört ätbeteende kunde leda till drastiska viktändringar, som i sin tur skulle leda till en viktökning över tid.

Den här studiens styrkor ligger i att dess sampel är stort och populationsbaserat. Dessutom kartlade den stört ätbeteende hos unga och medelålders vuxna personer, vilket i sig är ovanligt i och med att de flesta tvillingstudier och även andra studier i stört ätbeteende gjorts på barn och tonåringar. Att samplet bestod av såväl män som kvinnor är ytterligare en styrka, eftersom studierna om män och stört ätbeteende är mycket få. Till sist är den här studien den största som gjorts hittills vad gäller delad ärftlighet av stört ätbeteende och BMI.

Ett problem med föreliggande studie är att den mätte stört ätbeteende med enbart fem frågor. Ett annat var att trots att samplet innehöll män var dessa färre till antalet än kvinnorna. Tvillingmetoden i sig har också väckt mycket metodkritik när det gäller forskning om stört ätbeteende och andra psykosociala problem. Man kan t.ex. fråga sig hur säkert det faktiskt är att anta att det inte är enäggstvillingarnas större utseendemässiga likhet utan den genetiska likheten som leder till kopplingen i stört ätbeteende. Det här problemet har undersökts av Klump, Holly, Iacono, McGue, och Willson (2000), som bevisade att fysisk likhet tvillingar emellan inte är en modererande faktor vad gäller likheter i stört ätbeteende mellan tvillingar.

Föreliggande studie är viktig ur ett vårdvetenskapligt perspektiv, eftersom etiologin hos psykiatriska problem är ett viktigt fundament i behandling och preventivt arbete. Stört ätbeteende ses fortsättningsvis som något som så gott som helt orsakas av sociala faktorer, trots att de digra forskningsresultaten i dess ärftlighet torde ge tillräcklig grund för att man kunde börja betona dess genetiska bakgrund minst lika mycket som dess psykosociala (DeAngelis, 2002). Resultaten från studier som denna borde med andra ord anslutas till den information som ges åt såväl dem som lider av stört ätbeteende, dem som sköter om dessa och dem som utbildar vårdpersonal. I en studie om sjukskötarstuderande market man att betonandet av sociala faktorer i uppkomsten av ätstörningar i undervisningen ledde till att skötarna hade högre tendens att beskylla ätstörningspatienterna för deras problem (Crisafulli, Van Holle, & Bulik, 2008). Gruppen skötarstuderande som lärde sig om ätstörningar med betoning på ärftlighet hade mindre känslor av beskyllande gentemot patienterna med ätstörningar.

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