PART I

Eating Disorders

Anorexia Nervosa, Bulimia Nervosa, and Binge Eating Disorder
Chapter 1

**GENETIC AND BIOLOGICAL RISK FACTORS**

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**THE “OLD BIOLOGY OF EATING DISORDERS”**

Historically, sociocultural and family theories of etiology have dominated the scientific literature on eating disorders. There was certain sound logic to the belief that the pervasive emphasis on thinness as a symbol of beauty and control somehow “caused” eating disorders or that certain family interaction patterns were more likely than others to bring food and eating-related issues to the fore as a center of familial conflict. These explanations had considerable face validity—they seemed like common sense. However, they were not rigorously tested as true prospective risk factors. For decades, biological researchers have been working in the background of the scientific community of eating disorders. A small but dedicated group of researchers has continued to forge ahead with the notion that biology plays a substantial causal role in the etiology of anorexia nervosa (AN) and bulimia nervosa (BN).

**THE “NEW BIOLOGY OF EATING DISORDERS”**

In the past decade, genetic and biological research has moved to the forefront of our expanding knowledge about eating disorders. The findings are not ignorable, and they are forcing each of us to reshape our conceptualization of these disorders. Components of the “new biology” include research in the areas of epidemiology, genetic epidemiology, molecular genetics, neurobiology of feeding, neurobiology of eating disorders, genetics of obesity and thinness, and neuroimaging studies. In this chapter, I address how research on genetic epidemiology and genetics of eating disorders is forcing us to reframe our understanding of the balance of the contributions of genetic and environmental factors to the etiology of anorexia nervosa and bulimia nervosa.
HOW HAS GENETIC EPIDEMIOLOGY CHANGED OUR UNDERSTANDING OF THE ETIOLOGY OF EATING DISORDERS?

Over the past decade, a burgeoning of family, twin, and molecular genetic studies of eating disorders has shed new light on etiological factors associated with AN and BN. These findings have been sufficiently strong and adequately replicated to warrant the recommendation that all individuals in the field consider developing at least a passing familiarity with their meaning and their implications for etiology, prevention, and treatment of eating disorders. This chapter outlines the background for understanding the genetic epidemiological and molecular genetic approaches, presents current findings relevant to eating disorders, and suggests implications for prevention and treatment.

The Methods of Genetic Epidemiology: Family, Twin, and Adoption Studies

Three major research designs in genetic epidemiology allow for the delineation and quantification of the relative contribution of genes and environment to the etiology of complex behavioral traits (see Table 1.1). The first step is to determine whether a trait or disorder aggregates in families. This question can be addressed by the traditional family study, which determines whether there is a statistically greater lifetime risk of eating disorders in biological relatives of individuals who have an eating disorder in comparison to relatives of individuals without eating disorders. If no increased risk is observed, probability that the disorder is genetically influenced is low. The primary limitation of the family design is that genetics and environment are confounded. Therefore, if you find that a disorder or trait runs in families, the family study does not allow you to determine to what extent that familial pattern is due to genes and to what extent it is due to environment.

Two additional designs are possible that enable the disentangling of genetic and environmental effects, namely adoption and twin designs. Adoption studies are a social experiment in which the degree of similarity between an adoptee and his or her biological versus adoptive parents is compared. A greater similarity to biological parents

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| Family            | Case-control   | Familial?   | \[ a^2 c^2 \]  
|                   |                | e\^2        |
| Adoption          | Social experiment | Genes?     | a\^2         
|                   |                | Environment?| c\^2         |
| Twin              | Biological experiment | Genes?     | a\^2         
|                   |                | Environment?| c\^2         |

Note: \( a^2 \) = Additive genetic effects; \( c^2 \) = Common or shared environmental effects; \( e^2 \) = Unique environmental effects.
suggests genetic effects, whereas greater similarity to adoptive parents suggests envir-
ronmental effects. Although these are powerful designs, adoption is rare and the
method is complicated by a number of assumptions. Moreover, when studying rare
complex traits such as eating disorders, prevalence of the disorders is often too low to
draw meaningful conclusions from adoption studies.

Twin studies, in contrast, are a biological experiment. Monozygotic (MZ) or identi-
cal twinning occurs at some stage in the first two weeks after the first mitosis when the
zygote separates and yields two genetically identical embryos. Therefore, any differ-
ences between MZ twins who—for most intents and purposes share all of their genes—
provide strong evidence for the role of environmental influences (Plomin, DeFries,
McClearn, & Rutter, 1994, pp. 171–172). Dizygotic (DZ) or fraternal twinning results
from the fertilization of two ova by different spermatozoa. DZ twins are no more simi-
lar genetically than nontwin siblings and share—on average—half of their genes identi-
cal by descent. Thus, differences between DZ twins can result from genetic and/or
environmental effects.

The goal of the classical twin study is to use the similarities and differences between
MZ and DZ twin pairs to identify and delineate genetic and environmental causes for
a particular trait. Twin studies are one of the few quasi-experimental means to accom-
plish this goal in humans and are often the only practical approach.

Using structural equation modeling techniques, liability can be parsed to a trait
or disorder into three sources of variability: additive genetic effects ($a^2$), common or
shared environmental effects ($c^2$), and unique environmental effects ($e^2$).

**Additive Genetic Effects (Abbreviation A)**

Although a number of different types of genetic influences can be studied in theory
(e.g., dominance or epistatic effects), statistical power is usually low except for additive
genetic effects (Neale, Eaves, & Kendler, 1994). Additive genetic effects result from the
cumulative impact of many individual genes, each of small effect. The presence of $A$ is
inferred when the correlation between MZ twins is greater than the correlation between
DZ twins. If a trait were entirely due to additive genetic effects and could be measured
without error, the MZ:DZ correlation would be 1.0 and 0.5, respectively.

**Common Environmental Effects (Abbreviation C)**

Common environmental effects result from etiological influences to which both mem-
bers of a twin pair are exposed regardless of zygosity. Thus, common environmental ef-
fects contribute equally to the correlation between MZ and between DZ twins. In the
simplest case, if the correlations between MZ and DZ twins are both 1, the trait is en-
tirely determined by common environmental effects. Examples include the social class
and religious preference of the family of origin.

**Individual-Specific Environmental Effects (Abbreviation E)**

The second type of environmental effect results from etiological influences to which one
member of a twin pair is exposed but not the other. Thus, individual-specific environ-
mental effects decrease the magnitude of the correlation between both MZ and DZ
twins. In the simplest case, if the correlation between both MZ and DZ twins is 0,
the trait is entirely determined by individual-specific environmental effects. Examples
include one member of a twin pair being exposed to a traumatic experience not shared with the co-twin.

Qualitative characterizations such as the presence of C or the absence of A are useful, but quantifying the contributions of A, C, and E is more relevant. It is straightforward to scale the total variance of a trait to one and to use twin pair correlations to describe the proportions of variance due to A, C, and E. The proportion of variance due to A (additive genetic effects) is \( a^2 \) (also known as heritability or, more correctly, as narrow heritability in liability). The proportion of variance due to C is \( c^2 \), and the proportion due to E is \( e^2 \). The value of \( e^2 \) also incorporates measurement error. The values of \( a^2 \), \( c^2 \), and \( e^2 \) must sum to the total variance of one.

What Is Heritability? What Isn’t Heritability?

Perhaps because of unfamiliarity with the approach, twin studies can easily be misinterpreted. Heritability estimates are often quoted with little understanding of their meaning or of their limitations. Most importantly, there is not one true heritability estimate for any given trait or disorder. Heritability is a statistic that varies across populations and across time. Perhaps one of the most vivid examples of how heritability estimates of a trait can change over time emanates from a study of smoking behavior in male and female twins in Sweden. Kendler, Thornton, and Pedersen (2000) explored the pattern of twin resemblance for regular tobacco use in a population-based sample of Swedish twins. Results for males suggested both genetic and rearing-environmental effects, which, in the best-fit biometrical model, accounted for 61% and 20% of the variance in liability to regular tobacco use, respectively. For women, the pattern differed by birth cohort. In women born before 1925, rates of regular tobacco use were low and twin resemblance was influenced primarily by environmental factors. In later cohorts, rates of regular tobacco use in women increased substantially and heritability estimates were on par with those seen in men (63%). This study shows that heritable influences were detectable in females only after social constraints on female tobacco use were relaxed.

Allison and Faith (2000) outline a number of common misinterpretations of heritability. For example, a heritability of BN of 83% does not mean that 83% of the reason that people develop bulimia is genetic or that 83% of the people who have bulimia have a “genetic form” of bulimia. What it does mean is that approximately 80% (probably, more likely, 50% to 85% considering the confidence intervals) of the variance in liability to BN is due to genetic effects. More simply, your genes play a role in determining the extent to which you are liable to develop BN (or whatever the relevant trait may be).

LINKAGE AND ASSOCIATION STUDIES

If genetic effects appear to be important in the transmission of the disorder, linkage and association studies are next employed to determine the precise location, identity, and function of the genes that are implicated.

The two prominent molecular genetic designs are case-control association studies and linkage studies (Sham, 1998; Table 1.2). Case-control association studies are often
Genetic and Biological Risk Factors

viewed as alternative or complementary to linkage studies, which have yet to be as richly fruitful in the study of complex psychiatric traits in neuropsychiatry as they have with Mendelian disorders (Moldin, 1997; Risch & Zhang, 1996). Linkage studies (Craddock & Owen, 1996; Lander & Schork, 1994; Ott, 1991; Sham, 1998; Terwilliger & Goring, 2000) investigate correlations between a disease and inheritance of specific chromosomal regions in families, whereas association studies focus on differences in the frequency of specific genetic markers in groups of affected versus unaffected individuals (see Table 1.2).

The standard approach to association studies is to ascertain cases with a trait of interest and controls without the trait, obtain DNA samples, and genotype all subjects for a genetic marker believed to be of etiological relevance. Statistical analysis compares allele or genotype frequencies (Sasieni, 1997) in cases versus controls (Sham, 1998). As with any case-control approach, there are numerous sources of bias (Sackett, 1979); considerable care must be taken to ensure the proper matching of cases and controls. Fundamentally, cases and controls should represent “identical” samples from a single population except for the diagnostic differences. Confidence in case-control association studies wavers (Crowe, 1993; Gambaro, Anglani, & D’Angelo, 2000; Kidd, 1993; Risch & Zhang, 1996; Sullivan, Eaves, Kendler, & Neale, 2001). Association designs are particularly useful and powerful when prior knowledge of the pathophysiology of a trait suggests a number of candidate genes. However, the use of this design is controversial because of the risk of false positive findings when studying a sample that contains individuals of evolutionary diverse ancestry (Kidd, 1993). More often than not, seemingly exciting findings from association studies in neuropsychiatry are followed rapidly by a series of nonreplications (Moldin, 1997; Risch & Zhang, 1996; Stoltenberg & Burmeister, 2000).

Linkage studies can be used in gene discovery with a sufficiently large number of multiplex pedigrees or extreme sibling pairs (Allison, Heo, Schork, Wong, & Elston, 1998). Anonymous genetic markers scattered across the genome can identify the chromosomal regions that may contain genes that contribute to the trait of interest. The strength of this design is tempered by the relatively low power (Risch & Merikangas,
APPLICATION OF GENETIC EPIDEMIOLOGY AND MOLECULAR GENETICS TO EATING DISORDERS

Family Studies of Eating Disorders

A series of large, well-controlled family studies of eating disorders now exists. The vast majority of controlled family studies (Gershon et al., 1983; Hudson, Pope, Jonas, Yurgelun-Todd, & Frankenburg, 1987; Kassett et al., 1989; Lilenfeld et al., 1998; Strober, Freeman, Lampert, Diamond, & Kaye, 2000; Strober, Lampert, Morrell, Burroughs, & Jacobs, 1990) have found a significantly greater lifetime prevalence of eating disorders among relatives of eating-disordered individuals in comparison to relatives of controls. Moreover, several studies have found increased rates of both AN and BN (i.e., coaggregation) in relatives of individuals with AN as well as individuals with BN, compared to rates among relatives of controls (Gershon et al., 1983; Hudson et al., 1987; Kassett et al., 1989; Strober et al., 1990, 2000), suggesting that AN and BN share transmissible risk factors. Moreover, relatives of individuals with AN and BN have also been found to have a significantly increased rate of subthreshold eating disorders compared to relatives of controls (Lilenfeld et al., 1998; Strober et al., 2000), suggesting that the eating disorders do not “breed true” but are expressed in families as a broad spectrum of eating-related pathology. Woodside, Field, Garfinkel, and Heinmaa (1998) showed a tendency for AN to cluster more in families of probands with AN, possibly suggesting some specificity of clustering for AN.

In summary, family study data reveal an elevation in the lifetime prevalence of eating disorders among the relatives of people with eating disorders. In addition, the coaggregation in families of AN, BN, and milder eating disturbances suggests shared etiologic factors across these conditions.

Twin Studies of Eating Disorders

The goal of the classical twin study is to qualify and quantify similarities and differences between MZ and DZ twin pairs to identify and quantify genetic and environmental causes for a particular trait. Given that MZ twins, for most purposes, share all of their genes and DZ twins share, on average, half of their genes, any excess concordance in MZ twins over DZ twins suggests a genetic contribution to liability to the disorder. Conversely, any differences between MZ twins provide strong evidence for the
role of environmental influences (Plomin et al., 1994, pp. 171–172), whereas differences between DZ twins can result from genetic and/or environmental effects. More complicated statistical modeling allows parsing of the variance in liability to illness into three sources: additive genetic effects ($a^2$), shared environmental effects ($c^2$), and unique environmental effects ($e^2$). Additive genetic effects reflect the cumulative impact on a trait of many individual genes, each of which has a relatively small individual effect on the behavioral phenotype. The presence of $a^2$ is inferred when the correlation between MZ twins is greater than the correlation between DZ twins. By contrast, common environmental effects reflect etiological influences to which both members of a twin pair are exposed, regardless of zygosity. Examples of such effects include the social class and religious preference of the family of origin. Unique environmental effects, on the other hand, result from etiological influences to which one member of a twin pair is exposed but not the other and contribute to differences between members of a twin pair. Examples include one member of a twin pair being exposed to a traumatic experience not shared with the co-twin.

One of the key caveats to the twin study is the assumption of equal environments (EEA), which posits that MZ and DZ twins are equally correlated for their exposure to environmental influences that are of etiologic relevance to the trait under study (Plomin et al., 1994). That is, MZ twins are no more likely to have received similar exposure to an environmental factor that may play a causal role in eating disorders. We know that, in many cases, the environments shared by MZ twins are more similar than the environments shared by DZ twins. One vivid example is that MZ twins are more often dressed alike than DZ twins. Although this suggests a more correlated environment in MZ than DZ twins, the relevant point is that this dimension is not one that is assumed to be of etiological relevance to eating disorders. No extant data suggest that being dressed like your twin increases your risk of developing an eating disorder. Violations of the EEA are critical only when the violation occurs in domains that are relevant to the etiology of the trait.

If the EEA is violated, the greater resemblance of MZ twins in comparison to DZ twins could actually be due to environmental factors. A violation of the EEA does not necessarily invalidate the results of a twin study but may influence the magnitude of the estimated genetic and environmental components. Studies of the EEA concerning eating disorders suggest that this assumption has not been violated in twin studies (Bulik, Sullivan, Wade, & Kendler, 2000; Kendler, Neale, Kessler, Heath, & Eaves, 1993; Klump, Holly, Iacono, McGue, & Willson, 2000; Sullivan, Bulik, & Kendler, 1998).

**Twin Studies of Anorexia Nervosa**

Beyond isolated case reports, the first systematic study of clinically ascertained twins with AN (Holland, Hall, Murray, Russell, & Crisp, 1984; Holland, Sicotte, & Treasure, 1988; Treasure & Holland, 1989) found that the concordance for MZ twins was substantially greater than for DZ twins. Reanalyses of these data (assuming a population prevalence of AN of 0.75%) revealed evidence of familial aggregation with parameter estimates of 88% for $a^2$, 0 for $c^2$, and 12% for $e^2$. In short, the observed familial aggregation for AN appears to be influenced most strongly by additive genetic effects; however, the estimates were rather imprecise given the small sample size.
Population-based studies of AN are difficult to conduct given the relatively low prevalence of the disorder. There have been three twin studies of AN. Wade, Bulik, Neale, and Kendler (2000) derived heritability estimates for AN in the context of studying the nature of the comorbid relationship between AN and major depression. The heritability of AN was estimated to be 58%, although the authors could not rule out a contribution of shared environment to the liability to AN. Kortegaard, Hoerder, Joergensen, Gillberg, and Kyvik (2001) conducted a twin study on 34,142 Danish twins based on self-reported diagnosis of AN. They derived heritability estimates of 0.48 and 0.52 for narrow and broad definitions of AN. Finally, Klump, Miller, Keel, McGue, and Iacono (2001) estimated the heritability of broadly defined AN to be 0.74 in 17-year-old female twins, with the remaining variance accounted for by individual-specific environmental effects.

On balance, we can conclude from family studies (see Lilenfeld, Kaye, & Strober, 1997, for a review) that AN is familial. In addition, the preliminary twin studies, each of which carries its own unique shortcomings, suggest that the familiality is accounted for primarily by additive genetic effects. However, the jury is still out. The definitive resolution of the independent contribution of genetic and shared environmental factors to the observed familiality of AN will require more ambitious collaborative efforts to obtain larger sample sizes with sufficient statistical power.

**Twin Studies of Bulimia Nervosa**

Twin studies of BN have been more successful given the higher population prevalence of the disorder. Initial case series of twins with BN revealed consistently greater concordance for BN in MZ than DZ twin pairs (Fichter & Noegel, 1990; Hsu, Chesler, & Santhouse, 1990; Treasure & Holland, 1989). Pooling data from these case series for twin modeling and assuming a population prevalence of BN of 2.5% revealed evidence of familial aggregation with 47% of the variance accounted for by additive genetic effects, 30% by shared environmental effects, and 23% by unique environmental effects. However, the sample sizes were small and the estimates imprecise.

Population-based studies of BN have been conducted in the United States (Bulik, Sullivan, & Kendler, 1998; Kendler et al., 1991) and Australia (Wade, Neale, Lake, & Martin, 1999; Wade, Martin, et al., 1999) and via self-report diagnoses in Denmark (Kortegaard et al., 2001). The studies that have estimated the heritability of BN based on a single occasion of measurement suggest a moderate contribution of additive genetic effects, a negligible contribution of shared environmental effects, and a more substantial contribution of unique environmental effects to liability to BN (Bulik et al., 1998; Kendler et al., 1991; Kortegaard et al., 2001). Although a marked improvement over the clinical series, these studies still had limited statistical power given the relatively low population prevalence of BN and given that the reliability of the diagnosis of BN tends to be poor, which can lead to underestimation of both $a^2$ and $c^2$ (Bulik et al., 1998).

Two studies have boosted statistical power by incorporating more than one occasion of measurement into the twin model (Bulik et al., 1998; Wade, Martin, et al., 1999). This approach controls for unreliability of diagnosis, increases power to detect both $a^2$ and $c^2$, and, therefore, provides the most reliable information concerning the nature and magnitude of genetic and environmental contributions to BN. In short, these two studies reveal
a markedly greater contribution of additive genetic effects to the liability to BN (59% and 83%, respectively), a negligible contribution of shared environment (0 in both studies), and a moderate contribution of unique environmental effects (41% and 17%). Although the parameter estimates for $c^2$ were 0, the confidence intervals did not completely rule out a contribution of shared environment. Results from these two studies confirm the central role of genetic factors in the observed familiality of BN.

In summary, from twin and family studies, we can conclude that BN is familial and that there appears to be a moderate to substantial contribution made by genetic factors and unique environmental factors to liability to the disorder. The contribution of shared environment is less certain but appears to be of lesser prominence than the effect of genes and of unique environment. A reasonable next step for twin studies is to determine the precise nature of the unique environmental effects that increase risk for developing BN.

**LINKAGE AND ASSOCIATION STUDIES IN EATING DISORDERS**

Given that family and twin studies point toward the involvement of genes in the etiology of eating disorders, it has been sensible to pursue linkage and association approaches to begin to identify relevant genes.

Several extensive reviews of association studies of eating disorders contain comprehensive coverage of this topic (Gorwood, Bouvard, Mouren-Simeoni, Kipman, & Ades, 1998; Hinney, Remschmidt, & Hebebrand, 2000; Tozzi, Bergen, & Bulik, 2002). In the absence of linkage information, the majority of association studies have chosen candidate genes based on function. Genes associated with systems that have been implicated in feeding and body weight regulation have been common targets—such as genes associated with serotonergic function, dopaminergic function, neuropeptides related to feeding function, and other genes related to control of energy expenditure and metabolic adaptation during fasting. Although several groups have pursued association studies in eating disorders and encouraging associations have been found, no single gene or set of genes has consistently emerged across studies as being strongly associated with either AN or BN.

Linkage studies of AN and BN have only begun to appear in the literature. Kaye et al. (2000) reported on a linkage study sponsored by the Price Foundation of 192 families with at least one affected relative pair with AN and related eating disorders. This study represented a collaborative effort across a number of clinical sites across North America and Europe. The initial scan of the entire sample yielded no significant linkage results. However, two additional approaches yielded significant linkage results. First, to reduce sample heterogeneity, the researchers restricted the linkage analysis to a subset of families in which at least two affected relatives had a diagnosis of restricting AN (severe food restriction without the presence of binge-eating or purging behavior). This approach was important because heterogeneity in a sample can reduce underlying linkage signals. In many ways, restricting AN represents a uniquely recognizable phenotype and one that is plausibly influenced by heritable biological factors. The restricting AN subset yielded evidence suggestive of the presence of an anorexia susceptibility locus on chromosome 1 (Grice et al., 2002).
In an additional novel approach, Devlin et al. (2002) incorporated selected behavioral covariates into the linkage analysis. The key covariates were drive for thinness and obsessionality. The inclusion of these covariates, providing an additional means to refine the phenotype, revealed several regions suggestive of linkage on chromosomes 1, 2, and 13.

A second multicenter, collaborative eating disorder study, also supported by the Price Foundation, recruited probands with purging-type BN and family members affected with either AN, BN, or ED-NOS (Bulik et al., 2003). When the entire sample (316 families) was analyzed, significant linkage was observed on chromosome 10; suggestive linkage was observed on chromosome 14. However, the clinical presentation of BN can vary substantially suggesting marked phenotypic heterogeneity. Of the core symptoms of BN, the frequency of vomiting has been shown to be a reliable (Wade et al., 2000) and heritable measure (Sullivan et al., 1998). Thus, the phenotypic heterogeneity of the sample was reduced by selecting families that had at least two individuals with an ED and with regular vomiting behavior. This phenotypic clarification resulted in an even stronger linkage signal on chromosome 10.

These two examples highlight the importance of our fully understanding the phenotypes we are using in genetic analyses. That is, it is highly unlikely that the human genome maps perfectly onto the diagnostic categories that currently exist in the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD). It is imperative that individuals familiar with the clinical syndromes continue to refine their definitions of the natural clusterings of traits and disturbances that make up these conditions. It is only through sophisticated and accurate phenotyping that we will be able to maximize the tools we have at hand for genetic analysis and move closer to identifying genes that contribute to liability to these conditions.

**IMPLICATIONS OF THESE RESULTS FOR DETECTION AND PREVENTION**

Although the implications of genetic epidemiological and genetic research on eating disorders for treatment may seem to rest far into the future, implications for prevention are more immediate. The clear data on the familiality of these disorders underscore the notion that offspring of individuals with eating disorders are indeed at greater risk than individuals in the general population for the development of eating disorders.

In general, global preventive efforts for eating disorders have been less than optimally successful. Although as yet untried, consideration should be given to the development of targeted prevention efforts aimed at individuals who are at known increased risk by virtue of their family history.

Although offspring of individuals with eating disorders may be at greater risk by virtue of their genes, the expression of that genetic predisposition is not inevitable. Whereas much research has focused on environmental factors that contribute to the development of AN and BN, we know much less about environmental factors that inhibit the expression of a genetic predisposition to eating disorders.

A particularly difficult issue for prevention of eating disorders in high-risk populations has to do with gene-environment correlations. Genotype-environment correlation arises when the exposure to positive or negative environmental influences is not randomly
distributed with respect to genetic differences. For example, girls who are genetically more prone to body dissatisfaction may tend to evoke more appearance-related comments from their parents or peers (evocative gene-environment correlation) and actively seek peers or activities that reinforce their focus on appearance (e.g., cheerleading or modeling; active gene-environment correlation). Another type of gene-environment correlation (“passive” gene-environment correlation) reflects the fact that children receive genotypes that are correlated with their family environment. This latter form of gene-environment correlation may be particularly thorny when dealing with prevention. Stated in another way, you receive your genes from the same individuals who create your environment. Moreover, the environment that they create for you is in part determined by their genotype. Concretely, imagine a father with a subthreshold eating disorder who has passed on this genetic predisposition to his daughter. In addition, he has contributed to an environment in the family that is highly appearance focused, obsessed with low body fat, and perfectionistic. Thus, the daughter is not only dealing with the impact of her inherited genotype, but also being raised in an environment that may facilitate the expression of that genetic predisposition.

Given that many women with eating disorders continue to suffer from subthreshold symptoms and cognitions even after formal recovery from the eating disorder, the environment they create may contribute to expression. Research efforts to help understand how mothers with histories of eating disorders can create healthy environments for their offspring is essential—especially because problems have been identified in mothers with a history of eating disorders in terms of adequate nutrition during pregnancy, feeding styles, and parenting (e.g., Mitchell-Gieleghem, Mittelstaedt, & Bulik, 2002; Waugh & Bulik, 1999).

**IMPLICATIONS OF THESE RESULTS FOR TREATMENT**

The implications of twin and genetic research on treatment may be less immediate, but they can be conceptualized on two entirely different levels. The first level is how this information impacts patients’ and their supporters’ perception of the illness. Clinically, many patients find this type of information to be liberating—especially those individuals who may have been accused of having these disorders simply by “choice.” In contrast, others may become mired in a sense of biological or genetic determinism and may find the struggle against the disorder harder knowing that there is a genetic component to its etiology.

An additional concern voiced by some parents is that genetics can be viewed as yet another form of “mother blaming”—one over which they have even less control. It is, therefore, important to develop a strategy for incorporating this knowledge in a helpful way into patients’ understanding of their disorder. This often includes heavy emphasis on the fallacy of genetic determinism. It remains critical to underscore that the presence of a genetic predisposition in no way guarantees expression of the trait.

The second level on which genetic studies can influence treatment will result only when genes have been identified that actually influence susceptibility to the disorders. Such genes may highlight pathways of which we are already aware that influence feeding behavior, mood, or temperament (e.g., serotonergic pathways) or of yet-undiscovered
biological pathways that may influence susceptibility to these disorders. The discovery of new pathways may then pave the way for new pharmacological agents to influence their function.

REFERENCES


