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AN EXAMINATION OF COMORBIDITY AND
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ANOREXIA NERVOSA AND ANXIETY DISORDERS:

AN EXAMINATION OF COMORBIDITY AND SHARED TRANSMISSION

By

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ABSTRACT

ANOREXIA NERVOSA AND ANXIETY DISORDERS:
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By

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Objective: The current study sought to examine the nature of the relationship between anorexia nervosa (AN) and anxiety disorders (AD). There were two aims: (1) to examine comorbidity of AN and AD; and (2) to determine whether AN and AD share a common diathesis by examining rates of eating and anxiety disorders in parents of probands with AN and AD. **Method:** Female probands were selected from the Minnesota Twin and Family Study. To examine comorbidity, rates of AD were compared between probands with AN (n = 36) and probands with no eating pathology (n = 287). As well, frequencies of eating and anxiety disorders were compared between parents of probands with AN (n = 31 moms, 27 dads), or an AD (n = 109 moms, 92 dads), and controls with no eating or anxiety disorders (n = 43 moms, 41 dads) using chi-square, prediction analysis, and odds ratios. **Results:** Increased rates of comorbidity were supported as probands with AN showed higher rates of anxiety disorders than probands with no eating pathology. There was also support for shared transmission; parents of probands with AN had increased rates of both eating and anxiety disorders, regardless of anxiety comorbidity in probands. The same was found in parents of probands with multiple AD. **Discussion:** Initial support was provided for shared transmission of eating and anxiety disorders. However, differences in rates of transmission across study groups indicate the need for future research to examine AN and AD families to more precisely define etiologic relationships between the two phenotypes.

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Anorexia Nervosa and Anxiety Disorders:

An Examination of Comorbidity and Shared Transmission

Anorexia nervosa (AN) is a disorder of unknown etiology which affects approximately 0.5 - 1.0 % of adolescent and young women over their lifetime (Hoek, 1993; Hsu, 1990). The protracted course of the illness (Herzog et al., 1999; Strober, Freeman, & Morrell, 1997), combined with a mortality rate greater than that of any other psychiatric disorder (Sullivan, 1995), makes it pertinent that research focus upon risk factors involved in the development of AN. Traditionally, researchers have focused on the intense social pressures for a thin figure in industrialized nations as the primary contributing factor to the onset of AN (Garner, Garfinkel, Schwartz, & Thompson, 1980). However, the great majority of females that are exposed to these pervasive pressures never develop AN. Therefore, it is apparent that there are other processes which predispose certain women to develop AN (Chatoor, 1999).

Other potential risk factors, such as other forms of psychopathology, are currently being investigated to determine if they contribute to the development of AN. The increased rates of certain psychiatric disorders in women with AN has long been recognized (Wonderlich & Mitchell, 1997). The most common comorbid disorders are depressive and anxiety disorders (Toner, Garfinkel, & Garner, 1988; Fornari et al., 1992; Herzog, Keller, Sachs, Yeh, & Lavori, 1992; Herzog, Nussbaum, & Marmor, 1996). Historically, researchers have minimized the elevated rates of anxiety disorders in order to emphasize the link between eating and depressive disorders (Fornari et al., 1992; Hudson, Harrison, Yurgelton-Todd, Jonas, & Frankenburg, 1987; Hudson, Pope, Jonas, & Yurgelton-Todd, 1983). However, the nature of the relationship between eating and

depressive disorders remains elusive, as studies have provided conflicting information regarding potential etiological associations (Strober, Lampert, Morrell, Burroughs, & Jacobs, 1990; Wade, Bulik, Neale, & Kendler, 2000; Logue, Crowe, & Bean, 1989). On the other hand, recent studies have suggested a common, genetically-mediated diathesis between eating disorders (ED), phobias and panic disorder (Kendler et al., 1995), and a similar association has been suggested for AN and childhood anxiety disorders (Keel, Klump, Miller, McGue, & Iacono, in preparation). Such findings highlight the potentially significant role anxiety disorders play in the development and maintenance of AN, and thus underscore the importance of examining these relationships further.

Comorbidity Between AN and Anxiety Disorders

The prevalence estimates for anxiety disorders in women with AN range widely, but are consistently higher than those found in the general population. In one sample of treatment-seeking women with restricting AN, 73% were diagnosed with a current comorbid Axis I disorder at intake (Herzog et al., 1992); 20% of them were diagnosed with a current anxiety disorder. Other studies assessing lifetime rates of anxiety have found that 46% of an outpatient sample (Fornari et al., 1992), and 35% (Braun, Sunday, & Halmi, 1994), 60% (Bulik, Sullivan, Fear, & Joyce, 1997), and 83% (Godart, Flament, Lecrubier, & Jeammet, 2000) of inpatient AN samples have met criteria for at least one anxiety disorder at some point during their lifetime. It should be noted that only these last two studies included childhood anxiety disorders, which may account for their higher rates of lifetime comorbidity. Since the onset of AN occurs in mid- to late-adolescence for most women (American Psychiatric Association, 1994), the vast majority of eating disorder patients have not yet passed through the period of risk for many adult anxiety

disorders, but have done so for the childhood disorders. Comorbidity studies which do not assess the presence of childhood anxiety disorders are therefore likely to be underestimating the true prevalence of lifetime anxiety disorders in women with AN.

One limitation of many of these comorbidity studies that use clinic populations is that comorbidity may be increased in subjects seeking treatment. Specifically, the likelihood of treatment seeking has been found to be increased when more than one disorder is present (Galbaud, Newman, & Bland, 1993). This sampling bias makes it difficult to determine whether the same extent of comorbidity actually exists in the general population. Nonetheless, population-based studies have found elevated rates of anxiety disorders in women diagnosed with AN (Keel et al., in preparation; Walters & Kendler, 1995), although rates have generally been lower than those obtained in clinic-referred samples. Consequently, the frequent co-occurrence of AN and anxiety disorders seems to also exist in non-treatment seeking samples.

Another criticism levelled at studies of comorbidity in AN is that the behavioural or affective symptoms of comorbid disorders may simply be secondary consequences of malnourishment (Toner et al., 1988). The direct physiological effects of starvation include increased depressive symptoms, nervousness and anxiety (Keys, 1948), thus the symptoms of anxiety seen in women with AN may simply be due to starvation. However, studies of long-term weight restored AN women have found lifetime rates of adult anxiety disorders of 47% (Toner et al., 1988) and 53% (Halmi et al., 1991), which are still considerably higher than those expected in the general population. Further, 58% of long-term recovered AN patients report having had a childhood anxiety disorder (Deep, Nagy, Weltzin, Rao, & Kaye, 1995). Finally, almost half of a sample of former

AN patients assessed seven years after they initially sought treatment met criteria for a current anxiety disorder diagnosis (Herpertz-Dahlmann, Beate, Wewetzer, Schulz, & Remschmidt, 1996). These results suggest that high rates of both lifetime as well as current anxiety diagnoses are found in women with a history of AN even when malnutrition is not present.

Another reason it is unlikely that symptoms of anxiety are simply manifestations of malnourishment is the finding that, in the majority of cases, the onset of the anxiety disorder precedes the onset of AN. Twenty-three to 72% of women comorbid for AN and an adult anxiety disorder report an earlier onset of the anxiety disorder (Braun et al., 1994; Toner et al., 1988). Childhood anxiety disorders are reported to have an earlier onset than AN in 79% of long-term recovered AN patients (Deep et al., 1995). When both childhood and adult anxiety disorders are taken into account, the numbers are even higher: 83% (Godart et al., 2000) to 90% (Bulik et al. 1997) of anorexic women report an antecedent onset of their anxiety disorder.

In summary, high rates of anxiety disorders are consistently found in women with a primary diagnosis of AN. These elevated rates exist in both clinical and community populations regardless of state of illness, often with the anxiety disorder developing prior to AN. These stable, predictive relationships between eating and anxiety disorders underscore the importance of understanding the nature of the comorbid relationship. Indeed, understanding this nature is likely to provide information about the development and maintenance of AN.

Comorbidity research, which was once mainly descriptive, is now attempting to apply explanatory models in order to elucidate the etiological significance of the co-

presentation of certain psychiatric disorders with AN (Wonderlich & Mitchell, 1997). Two specific models, and their respective variations, are supported by the research reviewed on AN and anxiety disorders thus far. The predispositional model states that a comorbid disorder precedes and increases the risk of developing AN. This model is supported by chronology findings suggesting that anxiety disorders predate the onset of AN in the majority of cases.

The second model, the common cause model, asserts that common environmental or genetic risk factors independently lead to the development of both AN and anxiety disorders (Wonderlich & Mitchell, 1997). In other words, this model posits that the comorbidity of these disorders is due to a common underlying diathesis. Research using twin and family study designs has begun to directly examine the common cause model by determining whether the co-occurrence of AN and anxiety disorders is due to common genetic or common environmental factors. However, before it can be determined whether genes contribute to the co-aggregation of AN and anxiety disorders, it is necessary to ascertain whether each of these disorders are heritable.

Evidence for the Heritability of AN

Accumulated evidence indicates that there is a substantial genetic component to AN. For instance, family studies have found that first- and second-degree relatives of AN probands show higher rates of eating disorders compared to relatives of normal (Gershon et al., 1983; Strober et al., 1990; Strober et al., 2000; Lilenfeld et al., 1998) and psychiatric controls (Strober, Morrell, Burroughs, Salkin, & Jacobs, 1985; Hudson et al., 1983). The prevalence of AN has been found to be roughly 11.3 times greater in relatives of AN probands than relatives of controls, while the prevalence of bulimia nervosa (BN)

has been found to be 4.2 times higher than that in relatives of controls (Strober, Freeman, Lampert, Diamond, & Kaye, 2000). Further, relatives of AN probands have a 7 to 12 times higher rate of eating disorders not otherwise specified (EDNOS) compared to relatives of control women (Lilenfeld et al., 1998). Elevated rates of all forms of eating pathology in relatives of AN probands highlight possible shared transmission of different forms of eating disorders (Strober et al., 2000; Lilenfeld et al., 1998). This underscores the importance of looking at all forms of eating pathology in any examination of familial transmission.

Taken together, findings suggest significant familial aggregation of AN, yet the nature of this aggregation cannot be determined from family studies. Genetic and/or environmental factors could potentially account for this familial clustering. However, recent twin study findings suggest that at least some of the aggregation is due to genetic factors.

Twin studies of AN have found higher concordance rates in monozygotic (MZ) relative to dizygotic (DZ) twins (Holland, Hall, Murray, Russell, & Crisp, 1984; Holland, Sicotte, & Treasure, 1988). Since MZ twins share all of their genes, while DZ twins share only half of their genes, higher concordance rates in MZ versus DZ twins implicate at least a partial influence of genes on a trait/disorder. A population-based study using the same data as the present study (Klump, Miller, Keel, McGue, & Iacono, 2001) found that concordance rates in MZ twins ranged from 29% to 43% for narrow and broad definitions of AN respectively, while no DZ twins were concordant for the disorder.

Heritability estimates for AN have also been consistently high. Population-based samples have found heritabilities ranging from 58% to 74% (Wade et al., 2000;

Kortegaard, Hoerder, Joergensen, Gillberg, & Kybik, 2001; Klump et al., 2001), and these estimates are even higher in a clinically-based sample (Holland et al., 1988). Moreover, symptoms of disordered eating, such as body dissatisfaction, drive for thinness, and weight preoccupation, also show high degrees of heritability (Klump, McGue, & Iacono, 2000; Rutherford, McGuffin, Katz, & Murray, 1993; Wade et al., 1999). These genetic factors appear to exert greater influence on eating attitudes after girls have gone through puberty (Klump et al., 2000; Klump, McGue, & Iacono, 2003).

In sum, considerable support exists for the influence of genetic factors on the development of AN once girls have passed through puberty. The abundance of research implicating the influence of genes in the development of AN suggests that part of the comorbidity between AN and anxiety disorders may be due to shared genetic factors.

Evidence for the Heritability of Anxiety Disorders

Research on anxiety disorders reveals a similar pattern of genetic influence. Children of parents with anxiety disorders are more likely to develop an anxiety disorder themselves than children of parents without an anxiety disorder (Beidel & Turner, 1997; Capps, Sigman, Sena, & Henker, 1996; Turner, Beidel, & Costello, 1987; Weissman, Leckman, Merikangas, Gammon, & Prusoff, 1984). Again, although this provides evidence for familial transmission, it is unclear from family studies whether this is due to genetic or environmental factors.

Twin studies, however, indicate that genetic factors account for some of the variance in anxiety disorders. The few twin studies that have been conducted have found higher concordance rates in MZ relative to DZ twins (Kendler, Neale, Kesslre, Heath, & Eaves, 1992; Torgersen, 1983). A recent meta-analytic review of the genetic

epidemiology of anxiety disorders yielded heritabilities of 43% for panic disorder and 32% for generalized anxiety disorder (GAD), and concluded that familial aggregation for both of these disorders as well as the phobias is largely due to genes (Hettema, Neale, & Kendler, 2001). It is important to note that when a range of anxiety disorders are examined in twin studies, MZ twins tend not to be concordant for the same anxiety disorder (Torgersen, 1983; Andrews, Stewart, Allen, & Henderson, 1990). This suggests that transmission of anxiety disorders is non-specific, such that the genetic vulnerability may predispose individuals to a range of anxiety-related pathologies rather than a specific disorder per se.

Transmission of AN and Anxiety Disorders

Since both AN and anxiety disorders demonstrate evidence of genetic transmission, and they co-occur with a high frequency, it is possible that they share an underlying genetic diathesis. Very few studies have examined the cross-transmission of AN and anxiety disorders. This cross-transmission can be examined in two ways. First, twin studies can be used to quantify the relative influence of common genetic and common environmental factors on the co-occurrence of two disorders, such as AN and anxiety disorders. Although this method provides the strongest evidence for cross-transmission, the large sample sizes needed for adequate statistical power are difficult to achieve.

The second method for examining cross-transmission is the family study, where the rates of a co-occurring disorder (i.e., an anxiety disorder) are examined in the relatives of an individual diagnosed with the primary disorder under study (i.e., AN). If

there are increased rates of both the co-occurring and primary disorder in the relatives, then there appears to be cross-transmission of the two disorders.

There are two important features which strengthen the conclusions that may be drawn from such a study. Firstly, it is important to stratify relatives based upon the proband's comorbidity status, and then compare rates of the comorbid disorder between relatives of probands with the comorbid disorder and relatives of probands without the comorbid disorder. This enables researchers to ascertain whether proband comorbidity accounts for the increased rates of the comorbid disorder in the relatives. In such a case, the rates of the comorbid disorder would only be elevated in the relatives of probands with a personal history of the comorbid disorder, and transmission of the primary and comorbid disorder would thus be independent. Equally elevated rates of the comorbid disorder in relatives, regardless of the comorbidity status of the proband, suggest shared transmission.

The second important feature that should be included in family studies of shared transmission is the use of a comparison control group consisting of relatives of probands with the comorbid disorder. They would be examined to determine if they showed elevated rates of the primary disorder. This allows for the substantiation of any suggested shared transmission.

In general, family studies have suggested that there is shared transmission between eating and anxiety disorders. For example, a study in which a single anxiety disorder (i.e., OCD) was examined in the relatives of probands with AN indicated that risk for anxiety disorders was significantly higher in AN proband relatives than in relatives of controls (Bellodi, Cavallini, Bertelli, & Chiapparino, 2001). Likewise,

another family study examining a wide range of anxiety disorders in relatives of AN probands found increased rates of obsessive-compulsive disorder, generalized anxiety disorder, panic disorder, and social phobia compared to relatives of control women (Lilenfeld et al., 1998). Risk for these disorders ranged from 2 to 5 times higher in relatives of AN probands than relatives of controls. However, when the probands were stratified by the presence or absence of the comorbid disorder, evidence of shared transmission was only cautiously suggested for social phobia (Lilenfeld et al., 1998). In other words, there is some evidence that AN and social phobia may share a common familial transmissible factor, which increases risk for both disorders.

There are a number of possible reasons that may explain why shared transmission was not found with the other anxiety disorders. One is the small sample size. This study had a sample size that, once stratified, may not have been large enough to detect cross transmission between AN and other anxiety disorders. Even the potential relationship between AN and social phobia could not be clarified because of the small sample size following stratification. Another potential explanation for the lack of shared transmission relates to the previously mentioned research suggesting that anxiety disorders do not breed true (Turner et al., 1987; Torgersen, 1983). In other words, transmission does not necessarily involve a specific anxiety disorder (i.e., social phobia is transmitted from father to daughter), but rather a non-specific vulnerability for anxiety disorders in general (i.e., anxiety proneness is transmitted that might translate into a social phobia, panic disorder, etc.). Consequently, stratifying by the presence of any anxiety disorder may have been better able to clarify relationships between AN and anxiety disorders.

A recent twin study has provided some of the strongest evidence of cross-transmission of eating and anxiety disorders by using a discordant MZ twin (i.e., one twin has the disorder, her co-twin does not) design to directly examine shared risk for these disorders (Keel et al., in preparation). The discordant twin method involves assessing the non-disordered co-twins of twins with a specific disorder for the presence of a comorbid disorder. Since MZ twins share all of their genes, if the co-twins of disordered twins have a higher incidence of the comorbid disorder compared with the co-twins of controls it can be concluded that transmission is shared between the two disorders.

In this study, the co-twins of ED twins were two times more likely to suffer from childhood anxiety disorders compared to non-eating disordered controls. Further, there were no differences in the rate of anxiety disorders between ED twins with or without a childhood anxiety disorder, suggesting possible shared transmission between the two. A strength of this study was its inclusion of a comparison group of anxiety disordered twins without eating pathology. Results showed that the non-disordered co-twins of the anxiety disorder twins were more likely to be diagnosed with an ED compared to controls. Although this study provides support for shared transmission of eating and anxiety disorders, its results cannot be generalized to all anxiety disorders since only childhood anxiety disorders were examined.

Only one other study has looked at the presence of anxiety disorders in the relatives of eating disorder (ED) probands, using the relatives of probands with an anxiety disorder (OCD) as a comparison group (Pasquale, Sciuto, Cocchi, Ronchi, & Bellodi, 1994). The eating disorder probands were included in analyses if they were diagnosed with AN, BN or both. In this study, familial risk for EDs was not significantly

different between relatives of OCD probands and relatives of ED probands. This lack of familial specificity indicates partial support for a common predisposition, or shared transmission, as relatives of ED and OCD probands were equally likely to exhibit a lifetime history of eating pathology. Moreover, rates of specific anxiety disorders (i.e., panic disorder with or without agoraphobia, GAD, and anxiety NOS) were similar across relatives of probands with both disorders as well, although rates of OCD were significantly higher in relatives of OCD probands than relatives of ED probands.

The design utilized in Pasquale et al. (1994) - including a comparison anxiety disorder group - maximizes the ability to draw conclusions about shared transmission, however there are a few limitations that constrain the strength of the results. First, the fact that shared transmission was not found for OCD could be related to the idea that OCD may belong to another class of psychiatric disorders rather than to anxiety disorders. Some controversy exists regarding the categorization of OCD as an anxiety disorder because it shows a strong association and overlap with other, non-anxiety psychiatric disorders (e.g., mood disorders, personality disorders, impulse control disorders) (Brown, 1998; Hudson & Pope, 1990). Accordingly, OCD may not be representative of all anxiety disorders and thus may not exhibit the same pattern of shared transmission as other anxiety disorders previously investigated. This hypothesis is corroborated by findings described above (Lilenfeld et al., 1998) that also showed a lack of shared transmission between OCD and AN, but found evidence of shared transmission between AN and social phobia.

Another problem with the Pasquale et al. (1994) study is that there was no control group with which to compare the rates of disorders found in the relatives of probands

with OCD or ED, so it is not possible to say if these rates were truly elevated above those found in the general population. A comparison group consisting of the relatives of probands with no eating or anxiety pathology would help to clarify whether there truly exists a common diathesis which increases risk for both AN and anxiety disorders. Finally, researchers did not control for proband comorbidity, which makes it difficult to clarify the nature of any transmission. As noted above, without stratification based upon proband comorbidity, it is difficult to determine whether the elevated rates of the comorbid disorder are simply due to the comorbidity status of the proband or due to a shared diathesis.

To summarize, findings suggest that there is shared transmission of AN with social phobia and childhood anxiety disorders. The existence of such a relationship with other anxiety disorders remains unclear. Family studies alone cannot determine whether genetic influences underlie the co-occurrence of these disorders, but findings from twin studies suggest that transmission both within and between AN and anxiety disorders appears to be at least partially mediated by genes. If this transmission is shared, as recent research findings suggest (Keel et al., in preparation), a common genetic vulnerability may be involved in the development of both AN and anxiety disorders. Results of recent twin research does indicate shared genetic transmission between BN and certain anxiety disorders (Kendler et al., 1995), suggesting that the same may be true for AN. Understanding possible genetic links between AN and anxiety disorders would provide some insight into the presently elusive etiology of AN and may aid in the prevention and treatment of the disorder.

Study Objectives

Overall Purpose

The present study sought to corroborate and extend previous findings on comorbidity and possible shared transmission by examining diagnoses in parents of probands with AN and anxiety disorders. Specifically, this study compared the frequencies of anxiety disorder and eating disorder diagnoses in the parents of probands diagnosed with either AN, an anxiety disorder, or with no eating or anxiety pathology. The use of parental diagnoses and a comparison anxiety disorder group allowed for the direct examination of the comorbidity models. As mentioned above, the co-occurrence of AN and anxiety disorders may be explained by a predispositional model or a common cause model (Wonderlich & Mitchell, 1997). In the predispositional model, it is expected that relatives of probands with AN will not show elevated rates of anxiety disorders unless the proband herself is also diagnosed with that disorder. In this case, anxiety likely serves as a risk factor, simply increasing the likelihood that AN will develop.

By contrast, the common cause model posits an opposing hypothesis, such that the prevalence of AN and anxiety disorders would be elevated in the relatives of individuals with AN and relatives of individuals with an anxiety disorder, regardless of whether the proband is comorbid for both disorders. This would suggest that the disorders share a common diathesis. The present study directly examined these hypotheses by comparing rates of eating and anxiety disorders between parents of probands with AN and parents of probands with anxiety disorders. Parents of AN probands were also stratified by the presence of an anxiety disorder in the AN probands.

Specific Aims and Hypotheses

The first specific aim of the proposed study was to examine comorbidity between AN and childhood and adult anxiety disorders. This was done by comparing rates of lifetime anxiety disorder diagnoses between probands with AN and control probands who comprised the remainder of the sample with no eating pathology. To increase statistical power, these groups were also compared on a continuous measure of anxiety pathology, namely the State-Trait Anxiety Inventory (Spielberger, Gonsuch, & Luschene, 1970). It was expected that probands with AN would exhibit higher rates of anxiety disorders and symptoms than control probands.

The second specific aim was to examine possible shared transmission between AN and anxiety disorders. Rates of anxiety disorders and eating disorders were compared in parents of AN probands, parents of probands with any childhood or adult anxiety disorder, and parents of probands with no eating or anxiety pathology. Roughly equivalent rates of ED and anxiety disorders between the parents of AN twins and the parents of anxiety disorder twins, with both of these rates exceeding those of the parents of controls, would suggest that there is shared transmission of anxiety with AN.

The final specific aim was to directly compare the predispositional and common cause models by stratifying parents of the AN probands based upon the presence or absence of an anxiety disorder in the AN proband. Increased rates of anxiety disorders in the parents of AN probands, regardless of the comorbidity status of the proband, would support the common cause model of comorbidity and disprove the predispositional model. By contrast, the predispositional model would be supported if the parents of AN probands with a comorbid anxiety disorder had significantly increased rates of anxiety

disorders compared to the parents of probands without a personal history of anxiety disorders. Based upon the evidence supporting the involvement of genetic influences both within and between disorders, it was expected that the common cause model would best explain relationships between eating and anxiety disorders.

This study has a number of strengths that improve upon previous research in this area. First, no study to date has compared familial transmission of eating and anxiety disorders in probands with an eating disorder versus probands with a wide range of childhood and adult anxiety disorders. The use of this family study design allowed for the determination of which comorbidity model best explained the relationship between AN and anxiety disorders. Second, the sample is population-based, circumventing the treatment-seeking bias discussed earlier. Third, all subjects (i.e., AN, anxiety disordered, and control subjects) were ascertained from the same sample, decreasing sample heterogeneity that can result from sampling from several populations. Fourth, all probands fell within a relatively narrow age range, which is important since both AN and specific anxiety disorders have well-defined ages of onset. Thus, all women have had the same amount of time to develop the disorders under study. Finally, both categorical and continuous measures of eating and anxiety pathology were used. Examining both phenotypes increased our statistical power to detect significant shared effects.

Method

Participants

The sample is composed of a cohort of female probands (n = 672) who were followed longitudinally over two assessment periods. Data on the probands were first collected at an intake assessment (conducted when the probands were roughly age 17)

and then again at a follow-up assessment (conducted three years later at age 20). This sample is from the Minnesota Twin Family Study (MTFS), which is a population-based, longitudinal study of the development of substance use and related behaviors in same-sex male and female twins and their parents. When only one parent could participate in the study, data was usually collected on the mother; twins were not included when neither parent could participate.

Minnesota state birth records were used to determine families eligible for recruitment. These included families with live twin births, except when the following exclusionary criteria were met: (a) the family lived farther than a day's drive from the University of Minnesota's Minneapolis campus; (b) the twin pair had a physical or mental handicap that would preclude them from completing the self-report and interview assessments; or (c) the twins had been adopted. Other exclusionary criteria have been detailed elsewhere (Iacono, Carlson, Taylor, Elkins, & McGue, 1999). These families were then located through public databases such as telephone directories and drivers license registrations. Overall, the MTFS has successfully located more than 90% of twin births in the state of Minnesota in a given year.

The study was described in detail to all potential participants. Written informed consent was then obtained from all participants who were at least 18 years of age. Underage participants instead provided informed assent, while written informed consent was obtained from their parents.

In analyses examining specific aim #1 (i.e., examining comorbidity between AN and anxiety), the AN probands and a control group composed of the remainder of the sample with no eating pathology was examined. In analyses for specific aim #2, to

examine shared transmission between eating and anxiety disorders, the parents of probands with AN, anxiety disorders, and a control group with no eating or anxiety pathology were included. Thus, to reiterate, for the first analysis on comorbidity, two subject groups were examined: (1) probands with AN syndrome (n = 36; see details below), which included five pairs of concordant twins (i.e., both twins have the disorder); and (2) control probands with no eating pathology (n = 287). For the second analysis examining shared transmission, three subject groups were included: (1) parents of probands with AN syndrome (n = 31 moms and 28 dads); (2) parents of probands with any form of anxiety disorder (n = 109 moms and 92 dads); and (3) parents of probands with no eating or anxiety pathology (n = 43 moms and 41 dads).

Parents included in the AN group had at least one twin with the disorder. Anxiety disorder parents were selected for inclusion on the basis of having at least one twin with a lifetime diagnosis of one or more of the following: overanxious disorder, separation anxiety disorder, agoraphobia, agoraphobia without panic disorder, panic disorder with or without agoraphobia, generalized anxiety disorder, specific phobia or social phobia. Parents of twins who had an eating disorder *and* an anxiety disorder were included in the AN parent group, as were parents who had one twin with an eating disorder and the other twin with an anxiety disorder. Parents of twins with a BN or binge eating disorder (BED) diagnosis were excluded from analyses, given that the relatives of women with these disorders are at increased risk of having an eating disorder themselves (Lilenfeld et al., 1998; Strober et al., 2000).

The control group for the first specific aim (i.e., controls with no eating pathology) included all twins who did not meet criteria for threshold or subthreshold (one

symptom short) AN, BN, or BED. For this first analysis, one twin from each eligible pair was randomly selected for inclusion in the control group to ensure independent observations within groups. Control probands for the second specific aim (i.e., controls without eating or anxiety disorders), included all twin pairs without eating or anxiety disorder symptomatology. In both cases, controls were allowed to meet criteria for other psychiatric diagnoses (e.g., depression, ADHD) in order to provide a sample that was most representative of the population.

Measures

Eating Disorder Diagnoses and Characteristics. The Eating Disorders Structured Clinical Interview (EDSCI) was used to assess DSM-IV eating disorder diagnoses. This semi-structured clinical interview is based upon the eating disorders module of the Structured Clinical Interview for DSM Axis I Disorders (SCID I; Spitzer, Williams, & Gibbon, 1987), and was developed by MTFS researchers to assess anorexia nervosa, bulimia nervosa, and binge eating disorder.

A revised version of the Eating Disorders Inventory (EDI; Garner, Olmstead, & Polivy, 1983) was used to assess self-reported eating attitudes and behaviors. This 30-item, computer-administered Minnesota Eating Disorder Inventory (M-EDI; Klump et al., 2000; von Ranson, Klump, Iacono, & McGue, submitted) was developed by MTFS researchers to facilitate use with a preadolescent population, as the MTFS assesses a younger cohort of female twins not included in these analyses. Following factor analysis (Klump et al., 2000), four distinct subscales emerged: (1) Body Dissatisfaction, which assesses body shape and size dissatisfaction; (2) Weight Preoccupation, which assesses preoccupation with dieting, weight, and the pursuit of thinness; (3) Binge Eating, which

assesses the tendency to engage in, or think about, overeating; and (4) Compensatory Behaviour, which assesses the tendency to use or consider using compensatory methods of weight control (e.g., self-induced vomiting, misuse of laxatives). In addition, an M-EDI Total Score assesses current overall eating pathology. High M-EDI scores reflect greater eating pathology.

All M-EDI scales have adequate psychometric properties, with Cronbach's alphas ranging from .65 - .89 (Klump et al., 2000; von Ranson et al., submitted). Item analysis of these subscales indicates that the factor loadings for the M-EDI are highly similar to those of the original EDI (Klump et al., 2000). The stability across time is also similar between the two instruments, as indicated by the M-EDI's three-year stability coefficients of .31 to .60 (Klump et al., 2000; von Ranson et al., submitted) compared to the EDI's one-year correlations ranging from .44 to .75 (Garner, 1991). In addition, the M-EDI subscales show high discriminatory ability between women with eating disorders and non-eating disordered controls (von Ranson et al., submitted).

Anxiety Disorder Diagnoses and Characteristics. The Diagnostic Interview For Children and Adolescents – Revised (DICA-R; Reich & Welner, 1988) was used to assess the DSM-III-R childhood anxiety disorder diagnoses of overanxious and separation anxiety disorder. Other DSM-III-R anxiety disorders, such as social and specific phobias, generalized anxiety, PTSD, panic disorder with or without agoraphobia, agoraphobia, and agoraphobia without panic disorder were assessed with the SCID I (Spitzer et al., 1987).

The State-Trait Anxiety Inventory (Spielberger et al., 1970) was used to assess self-reported anxiety. This 40-item scale is well-established as a measure of both

transitory (state) and stable (trait) levels of anxiety. Both the state and trait subscales consist of 20 statements, with 4-point Likert scale responses. On the state scale, respondents evaluate how they are feeling at that very moment, while on the trait scale, responses are made regarding how they generally feel. Higher scores reflect greater levels of state or trait anxiety. This scale has been validated on a number of different populations, and norms are available for working adults, college and high school students (Spielberger et al., 1970). Stability coefficients are quite high for the trait scale (range = .65 - .86), while those for the state scale are rather low (range = .16 - .62), reflecting its sensitivity to situational factors which exist at the time of testing (Spielberger, 1983). The scale correlates well with other measures of anxiety (Spielberger et al., 1970), supporting its validity. Moreover, when individuals were assessed with the STAI prior to and following a stressful situation, only the state measure showed any change, supporting the differentiating power of the STAI (Metzger, 1976). Probands were administered both the state and trait subscales, while parents only completed the trait subscale.

Diagnostic Procedures

All of the structured interviews were administered face-to-face by trained clinical interviewers, with separate interviewers conducting assessments of co-twins and their parents. A clinically trained diagnostic team then evaluated the item coding. The initial coding of items and the diagnostic evaluations for parents and co-twins were conducted blind to the diagnosis of the proband. Computer algorithms based upon DSM-III-R (for anxiety disorders) and DSM-IV (for eating disorders) criteria then generated diagnoses.

For the anxiety disorders, participants were considered to be positive for the disorder if they met full DSM-III-R criteria. All probands who met criteria for AN

syndrome at intake or follow-up were included in analyses. The AN syndrome diagnostic category includes participants who met full DSM-IV criteria for AN, were one symptom short (note that the one symptom short could not be, by definition, low body weight), or were subthreshold for the disorder. A subthreshold diagnosis was given when a subject was $\leq$ 90% ideal body weight (IBW), and had a disturbed body image (intense fear of gaining weight or becoming fat, disturbance in perception of body size or shape, or undue influence of body shape or weight on self-evaluation), and an M-EDI score above the mean (11.0) of probands who met full criteria for anorexia nervosa.

The eating disorder criteria differed for parental data. Fathers were not assessed for eating disorders, and only those mothers who met full DSM-IV criteria for an eating disorder (anorexia nervosa, bulimia nervosa, or binge eating disorder) or fell one symptom short were deemed to have a positive diagnosis. Subthreshold diagnoses could not be given for parents, as the M-EDI assesses current eating pathology, and most mothers who were positive for a lifetime diagnosis of eating disorder would have experienced the disorder in the past.

Interrater reliability of assigned diagnoses was determined at intake by comparing the diagnostic evaluations of two independent consensus teams. Non-eating disorder diagnoses had relatively high kappa coefficients: 0.77 for separation anxiety disorder; 0.92 for overanxious disorder; 0.93 for panic disorder; 0.79 for agoraphobia; 0.85 for panic disorder with agoraphobia; 0.74 for panic disorder without agoraphobia; 0.80 for social phobia; and 0.75 for simple phobia. Reliability information on GAD was not available because of its low prevalence rate. The kappa coefficient for AN was slightly lower at .62. To ensure the validity of AN diagnoses, two MTFS researchers reviewed

each case individually after its initial review, and added the criterion of minimum M-EDI scores (as described above).

Statistical Analyses

A p value of .05 was used for all analyses. Statistical analyses for each specific aim were as follows:

Specific Aim 1: In order to examine comorbidity of eating and anxiety pathology, frequencies of anxiety disorders were compared between the AN syndrome proband group and the control group with no eating pathology using a chi-square test of independence. Fisher's exact test was implemented when the sample size for a particular group was less than ten. In addition, STAI scores were compared between AN syndrome probands and control probands using independent samples t-tests.

Specific Aim 2: The cross-transmission of anxiety and eating disorders was examined by:

(a) comparing frequencies of anxiety disorders, eating disorders, and 'no eating or anxiety diagnoses' between the mothers and fathers of AN syndrome probands, anxiety disorder probands, and control probands with no eating or anxiety pathology. Again, chi-square tests were implemented to analyze the diagnostic data, using Fisher's exact test where appropriate. These initial analyses were followed by prediction analyses for cross-classifications (von Eye, 1997) to test the specific hypothesis that AN and anxiety disorder parents would have elevated frequencies of eating and anxiety disorders compared to the control parents.

Prediction analysis is a statistical procedure which allows for the examination of specific sets of point predictions between predictor and outcome variables. It is similar to

chi-square in that it examines associations between categorical variables, but it is a more precise and powerful test because it allows one to make direct predictions regarding associations. Prediction analysis provides an overall test of the significance of the model, or how well the predictions were supported by the data, and also tests the success of predictions for each individual variable. Negative prediction success suggests that the predictions were less accurate than would be expected from chance. On the other hand, positive prediction success indicates that there was a greater reduction in the error rate than would be expected by chance, and therefore that the predictions made correspond to the actual associations between predictor and outcome variables found in the data. The specific predictions that were tested were that parents of probands with AN or an anxiety disorder would have increased rates of both eating and anxiety disorders, while parents of controls would have increased rates of 'no eating or anxiety diagnoses'.

Odds ratios were also calculated to determine the likelihood of parents of AN and anxiety probands having an eating or an anxiety disorder diagnosis compared to that of the controls. Odds ratios allow for direct comparisons to be made between the diagnostic groups and non-diagnostic groups (controls), and unlike prediction analysis, odds ratios do not rely upon base rates.

In order to control for the possible effects of proband comorbidity, these analyses were conducted on the entire AN syndrome group, and also with the AN group divided into those with a comorbid anxiety disorder and those without a diagnosed anxiety disorder. Here, the shared transmission hypothesis asserts that AN parents would show elevated rates of anxiety disorders regardless of whether the AN proband had a personal history of an anxiety disorder.

(b) comparing scores on continuous measures of eating and anxiety pathology (M-EDI and STAI-Trait) between parents of probands with AN, anxiety disorders, and control probands using analysis of variance (ANOVA) with follow-up Tukey's post-hoc t-tests.

Results

Analysis 1: Examining Comorbidity in Proband Sample

For Analysis 1, rates of anxiety disorders were compared between probands with AN and the remainder of the proband sample using chi-square analyses to examine whether AN women have higher rates of anxiety disorders than a general population sample with no eating pathology (see Table 1). The results indicate that women with AN had higher rates of PD, PD without agoraphobia, specific phobia, GAD, and 'any anxiety disorder' than control probands without any eating pathology. There was also a trend towards higher rates of overanxious disorder and PTSD in probands with AN. No significant differences in the rates of the other anxiety disorders emerged.

Anxiety pathology was further examined by comparing mean scores on the STAI between probands with AN and the rest of the sample. T-test results, as shown in Table 2, indicate that there are no differences in scores on either the State or Trait subscales of the STAI for women with AN versus controls with no eating pathology. An additional analysis, shown in Table 3, was performed to determine whether a high rate of anxiety disorders amongst controls could account for the lack of differences. However, when women with anxiety disorders were removed from the control sample, there were still no differences in STAI scores between women with AN and controls without eating or anxiety diagnoses.

Analysis 2: Examination of the cross-transmission of eating and anxiety disorders.

For Analysis 2, rates of eating and anxiety disorders were compared in parents of probands with either AN, an anxiety disorder, or no eating or anxiety pathology in order to determine whether there is shared transmission between eating and anxiety disorders. If shared transmission exists, rates of eating and anxiety disorders would be greater than expected for parents of probands with either an eating or an anxiety disorder. Frequencies of all parental eating and anxiety disorders are depicted in Table 4. Due to low rates of individual disorders, analyses were not performed on separate diagnoses. Instead, all eating disorders were combined into an 'ED' group, and individual anxiety diagnoses were combined into an 'anxiety disorder' group.

Diagnostic data for these combined groups are presented in Table 5. The chi-square analysis examining rates of ED, anxiety disorders and 'no eating or anxiety diagnoses' between parents of probands with AN, probands with an anxiety disorder, and control probands was significant, suggesting that there were differences in frequencies of eating and anxiety disorders and 'no eating or anxiety diagnoses' between the three parental groups. The overall model for prediction analysis was also significant, indicating that parents of probands with AN and parents of probands with an anxiety disorder had increased rates of both EDs and anxiety disorders, while parents of controls had a greater than expected frequency of 'no eating or anxiety diagnoses'. The reduction in error compared to that expected randomly for each individual hypothesis was 29.0% for parents of probands with AN, 1.1% for parents of probands with an anxiety disorder, and 22.1% for parents of controls. Thus, the strength of the prediction varied between the

groups, with the predictions most strongly supporting the results found in parents of women with AN and parents of controls.

Odds ratios provide additional information regarding the prevalence of eating and anxiety disorders in parents of probands with AN or an anxiety disorder, compared to controls. Parents of probands with AN were 9.4 times more likely to have an ED and 2.3 times more likely to have an anxiety disorder compared to controls, with both results achieving significance. Odds ratios for parents of anxiety disorder probands did not reach significance, but they suggest that parents of probands with an anxiety disorder were more likely to have an ED, while they were not more likely to have an anxiety disorder. Similar to the prediction analysis findings, there is stronger support for shared transmission in parents of probands with AN. The weaker support in parents of probands with an anxiety disorder appears to be primarily due to a lack of familial transmission of anxiety disorders.

Comparable results were found for continuous measures of eating and anxiety pathology (see Table 6). Parents of probands with AN showed the highest levels of eating and anxiety pathology, as their mean scores were significantly higher than parents of controls on M-EDI Total Score, Binge Eating, and STAI-T. Parents of probands with AN and parents of probands with an anxiety disorder had higher mean scores on Weight Preoccupation than parents of control women. Together these results suggest some shared transmission of pathology that, similar to the diagnostic findings, is more strongly supported by parents of probands with AN. Overall, parents of probands with AN endorsed the most pathology on all scales, followed by parents of probands with an anxiety disorder, whereas parents of control probands had the lowest mean scores.

Proband Stratification

As noted above, parents in the AN group were divided according to comorbidity in the proband in order to ensure that elevated rates of eating and anxiety disorders in the AN parental group were not due to the presence of a comorbid anxiety disorder in the proband. As well, the lack of familial aggregation of anxiety disorders was an unexpected finding, and one possible explanation for this result was that differences in familial aggregation may exist between families with one versus multiple anxiety disorder diagnoses. Therefore, anxiety disorder probands were also stratified by comorbidity and analyses were re-run on their parents. There were four resultant parent groups that included parents of probands with: (1) AN only; (2) AN and a comorbid anxiety disorder; (3) a single anxiety disorder; and (4) more than one anxiety disorder. Rates of EDs and anxiety disorders in these parents were then examined along with parents of controls (see Table 7). The chi-square indicates that there is a significant difference in frequencies of eating and anxiety disorders between parent groups.

The prediction analysis was also significant. This suggests that in general, parents of probands with AN or anxiety disorders had increased rates of both EDs and anxiety disorders, while parents of controls had a higher than expected frequency of individuals without an ED or an anxiety disorder. When examining the individual hypotheses, prediction error was reduced by 20.4% for parents of probands with AN only, 35.0% for parents of probands with AN and an anxiety disorder, and 33.5% for parents of probands with more than one anxiety disorder. However, there was negative prediction success for parents of probands with only one anxiety disorder, suggesting that the lack of shared

transmission previously found in parents of probands with an anxiety disorder was due to low rates for transmission of eating and anxiety disorders within this group.

These results are supported by odds ratio findings. They indicate that parents of probands comorbid for AN and an anxiety disorder were more likely to have an eating disorder or an anxiety disorder than parents of controls. Although these same analyses did not reach significance with parents of probands with AN only, the magnitude of the odds ratios suggest increased rates of both disorders. Parents of probands with two or more anxiety disorders also have increased rates of eating disorders and a trend towards higher rates of anxiety disorders compared to controls. Finally, parents of probands with only one anxiety disorder were not significantly more likely to have an eating disorder or an anxiety disorder.

Continuous M-EDI and STAI-T data on the stratified AN and anxiety sample is presented in Table 8. A review of the means for the M-EDI indicates that parents of probands with AN only, AN and a comorbid anxiety disorder, or multiple anxiety disorders had similarly high scores on Total Score and Weight Preoccupation. However, small sample sizes may have limited the ability to detect significant effects, as differences are only indicated between parents of probands with multiple anxiety disorders and parents of controls on these scales. On Binge Eating and Trait Anxiety, parents of probands with multiple anxiety disorders and parents of probands with both AN and an anxiety disorder had significantly higher mean scores than parents of controls. In general, these results concur with the diagnostic findings suggesting that the strongest rates of cross-transmission are found in parents of women comorbid for AN and an anxiety disorder or with multiple anxiety disorders. However, higher M-EDI scores,

although not significantly different from controls, also suggest increased transmission of eating pathology in parents of probands with AN only.

Discussion

The present study confirms past findings of high frequencies of anxiety disorders in women with AN. Moreover, the present findings also contribute to the scant literature on shared transmission between eating and anxiety disorders. Support for cross-transmission was indicated, as parents of probands with AN showed elevated rates of both eating and anxiety disorders which could not be entirely accounted for by proband comorbidity. Cross-transmission was also confirmed in parents of probands with an anxiety disorder when considering multiple anxiety diagnoses. Thus, cross-transmission of eating and anxiety disorders was apparent in both the AN and the anxiety disorder samples. These findings also attest to the importance of including a control anxiety disorder group, as different rates of transmission were noted between in the AN proband group and the anxiety proband group. The anxiety disorder comparison group provided important insight into factors which may influence transmission rates, such as comorbidity of anxiety disorders in both AN and anxiety disorder families.

Comorbidity of Eating and Anxiety Disorders in Probands

The present study corroborated previous findings of increased rates of anxiety disorders in individuals meeting criteria for AN syndrome. Nearly 50% of AN individuals in this sample met full criteria for a lifetime anxiety disorder. This rate is somewhat lower than those previously found in studies examining lifetime rates of both childhood and adult anxiety disorders in a treatment-seeking sample (Bulik et al., 1997; Godart et al., 2000). However, the present rates are considerably higher than those

obtained by researchers who only focused on adult anxiety disorders in population-based samples (Walters & Kendler, 1995) or treatment-seeking samples of AN patients (Braun et al., 1994; Fornari et al., 1992; Herzog et al, 1992). Thus, the combined use of a population sample, along with the inclusion of both childhood and adult anxiety disorders, may have provided a more accurate representation of rates of anxiety disorders for women with AN in the general population.

It is difficult to interpret the comparisons between women with AN and controls with no eating pathology for the individual anxiety disorders since many did not reach significance. The frequencies of most of the adult anxiety disorders are quite low, partly due to the young ages of the participants, which reduced the ability to detect statistically significant effects. Most previous studies of comorbidity included women who were at least approximately five years older than the present sample (Braun et al., 1994; Bulik et al., 1997; Deep et al., 1995; Halmi et al., 1991; Lilenfeld et al., 1998; Toner et al., 1988).

The only published study that used a community-based sample to examine anorexia and anorexic-like syndromes found increased rates of all of the anxiety disorders assessed within that study (GAD, PD, and phobias (undifferentiated)), although these rates differed between ED diagnostic spectrums (Walters & Kendler, 1995). The present study has produced an exact replication of those results, as higher rates of GAD, PD, and specific phobia were found in women with AN compared to controls. Moreover, the present study extended upon this previous community investigation by finding trends towards women with AN having increased rates of both overanxious disorder and PTSD.

Considering that women with AN had increased rates of anxiety disorders, it was somewhat unexpected that this finding did not extend to the continuous anxiety pathology

data. Neither state nor trait anxiety scores were significantly different between women with AN and control women with no eating pathology, even after removing control individuals who met criteria for an anxiety disorder. A previous study using the STAI found differences in scores between healthy controls and women with AN (Pollice, Kaye, Greeno, & Weltzin, 1997). It should be noted that the control women employed in this previous study were meticulously screened to ensure that they had no comorbid Axis I disorders, while the present control sample was only screened for eating and anxiety pathology. The use of completely clean controls maximizes the chances of observing differences across groups and increases the chances for significant effects when compared to analyses of unscreened controls.

Thus, in general, the present findings replicate previous results by confirming high frequencies of anxiety disorders in individuals with AN. The use of a population-based sample, along with the inclusion of both childhood and adult anxiety disorders, increases generalizability and provides more accurate estimates of comorbidity than those derived from purely clinically-based samples.

Cross-transmission of eating and anxiety disorders

The findings of the present study lend initial support to the possibility that there is cross-transmission of eating and anxiety disorders. Women with AN are more likely than controls to have parents with either AN or an anxiety disorder. After separating AN parents based upon the presence or absence of a comorbid anxiety disorder in their daughters, transmission rates are stronger in parents of women with both AN and an anxiety disorder; however there are trends suggesting that increased rates of eating and anxiety disorders also exist in parents of probands with AN only. It thus appears as

though the cross-transmission evident in parents of probands with AN cannot be accounted for solely by proband comorbidity.

In order to confirm cross-transmission, there must also be elevated rates of eating and anxiety disorders in the parents of probands with an anxiety disorder. Initially, this support was not found, as parents of probands with anxiety showed only a slightly increased rate of eating disorders, but not anxiety disorders. Levels of trait anxiety also were not elevated in parents of women with an anxiety disorder. However, when probands were divided into parents of probands with a single anxiety disorder versus those with multiple anxiety disorders, anxiety comorbidity in the proband was associated with increased eating and anxiety pathology in parents. Thus, the cross-transmission found in parents of probands with AN was confirmed in the anxiety disorder group when only the parents of probands with multiple anxiety disorders were considered.

These results attest to the importance of including a control anxiety group in any study of shared transmission between eating and anxiety disorders, as results from the ED group alone may provide an incomplete depiction of shared transmission between eating and anxiety disorders. Shared transmission cannot be fully supported unless it is confirmed in both the relatives of individuals with ED and those with anxiety disorders. Additional features of transmission, such as the influence of anxiety comorbidity, may only become apparent when such a comprehensive design is employed.

The lack of transmission of anxiety associated with single anxiety disorders was unexpected, as the familial transmission of anxiety disorders (Beidel et al., 1997; Hettema et al., 2001; Mancini, van Ameringen, Szatmari, Fugere, & Boyle, 1996) and anxiety pathology (Andrews et al., 1990; Stein, Jang, & Livesley, 1999) has received

considerable support. Having a relative with an anxiety disorder may increase one's risk of developing a different anxiety disorder (Andrews et al., 1990; Torgersen, 1983), and this lack of specificity in transmission was controlled for by examining all anxiety disorders in the parents of probands meeting criteria for any anxiety disorder. In spite of this, there was still no evidence of transmission in parents whose daughters were diagnosed with a single anxiety disorder.

Certain anxiety disorders may exhibit a greater genetic influence than others (Torgersen, 1983), and heritabilities for anxiety disorders only fall in the modest range (Hettema et al., 2001), which may have contributed to the lack of independent transmission. However, the finding that increased rates of transmission are associated with comorbidity raises the possibility that previous studies that examined clinical populations may have included many probands with multiple anxiety disorders. Treatment-seeking has been associated with increased comorbidity (Galbaud et al., 1993), and the use of clinical samples may have therefore resulted in increased anxiety disorder comorbidity and thus support for the familial aggregation of these disorders.

There are some potential explanations for the finding that transmission is associated with multiple, but not single, anxiety disorders. Anxiety disorders are the most common psychiatric disorders diagnosed in the general population (Pollack et al, 2002), so it is not particularly unusual to meet criteria for a single anxiety disorder during one's lifetime. However, meeting criteria for more than one anxiety disorder may represent a shift from a relatively normative diagnosis to a more severe condition. Certain influencing factors may be required to pass this threshold; perhaps genetic factors are involved in the development of a broad range of anxiety symptoms which are then

exhibited through comorbidity of anxiety disorders. Further, this increased heritability may account for the higher rates of eating disorders and general eating pathology in parents of probands with comorbid anxiety diagnoses as shared genetic factors may underlie the relationship between eating and anxiety disorders. Future studies of the transmission of anxiety disorders should examine familial aggregation and heritability for single versus multiple anxiety diagnoses to determine whether comorbidity does represent a greater genetic influence.

Another possibility is that higher levels of pathology in general lead to more pathology within families. Results here indicate that women who met criteria for more than one disorder, whether it was multiple anxiety diagnoses or AN and an anxiety diagnosis, were more likely to have parents exhibiting some form of pathology. Given that shared transmission of anxiety and mood disorders has also received support (Turner et al., 1987), attempts should be made to decipher whether there is true specificity in the transmission of eating pathology and anxiety disorders, or if high levels of pathology simply produce a non-specific vulnerability for a broad spectrum of psychiatric disorders.

Models of Comorbidity

One of the original objectives of the present study was to determine which model of comorbidity could best account for the relationship between eating and anxiety disorders. To recap, the two explanatory models for comorbidity of eating and anxiety disorders that were introduced earlier were the common cause model and the predispositional model. The common cause model purports that eating and anxiety disorders are independent disorders which share a common underlying diathesis, while the predispositional model asserts that high rates of comorbidity between eating and

anxiety disorders are due to increased risk for AN following the premorbid onset of an anxiety disorder (Wonderlich & Mitchell, 1997).

The results of the present study cannot be used to discount the predispositional model, as the results of the proband stratification were somewhat ambiguous. While the prediction analysis supported increased rates of eating and anxiety disorders in parents of probands with AN only, the odds ratios were not as definitive due to small sample sizes and the resultant broad confidence intervals. However, the odds ratios were of a large magnitude, so despite being imprecise estimates they suggest that parents of probands with AN only do have increased rates of eating and anxiety disorders. This conclusion is in line with the common cause model. Therefore, the trends towards increased rates of eating and anxiety disorders in parents of probands with AN despite proband comorbidity provide support for the common cause model, yet do not rule out the predispositional model as a explanation for comorbidity between eating and anxiety disorders. Additional family and longitudinal research is required in order to clarify the comorbidity model which can best account for the relationship between ED and anxiety disorders.

Conclusions and Study Limitations

In conclusion, these findings provide support for shared transmission of eating and anxiety disorders. Previous studies have used different designs to examine shared transmission, which has resulted in somewhat different conclusions (Keel et al., in preparation; Lilenfeld et al., 1998; Pasquale et al., 1994). The present study improved upon those conducted previously by combining anxiety disorders into a single entity, using a comparison anxiety disorder proband group as well as a control group without eating or anxiety pathology, and stratifying the proband group for the presence or absence

of a comorbid anxiety disorder. Despite the increased stringency of this design, some questions remain about the nature of the relationship between eating and anxiety disorders, and follow-up is required to further investigate shared transmission. All of these procedures, however, should be maintained in the future in order to provide consistency across studies so that stronger conclusions may be drawn regarding shared transmission.

Nonetheless, a number of limitations of the present study should be noted. First and foremost is the small sample size. AN is a relatively rare psychiatric disorder. A number of analyses approached but did not reach significance, and the small sample size may have contributed to the inability to detect significant effects. This study should be replicated with larger AN and control samples to replicate and clarify the present findings.

Another limitation is that some potentially important diagnostic information was not collected for this study. Specifically, OCD was not assessed. There appears to be a strong relationship between AN and OCD, as there are high rates of comorbidity in women with AN (Godart, Flament, Perdereau, & Jeammet, 2001) as well as women with OCD (Fahy, Osacar, & Marks, 1993), and first-degree family members of women with AN have increased rates of OCD (Lilenfeld et al., 1998). The single study in which proband stratification was used to examine the relationship between AN and OCD found that the increased rates of OCD in relatives of women with AN were due to proband comorbidity and not cross-transmission (Lilenfeld, 1998). However, this result has yet to be replicated, and the nature of the relationship between AN and OCD remains unclear.

In addition, no diagnostic information was collected on eating disorders (ED) in fathers. Although ED are quite rare in males, fathers of AN probands evidenced high levels of eating pathology on the M-EDI (data not shown). Eating disorder diagnostic information would have therefore supplemented these continuous data and increased sample sizes for the odds ratios, which may have lead to more definitive support for shared transmission. Finally, first degree relatives other than parents were not included. Although another study found similar results using the co-twins of the probands in the present sample (Keel et al., in preparation), additional information from other first-degree relatives, such as non-twin siblings, would provide a more thorough analysis of cross-transmission.

As a final note, due to their young ages, many of the participants have not yet passed through the periods of risk for eating disorders or adult anxiety disorders. Women in the anxiety disorder group may go on to develop an eating disorder, and some women in the eating disorder group may develop an anxiety disorder at some point in their lifetime. Consequently, it is possible that the data on both comorbidity and transmission may change over time, as crossover may occur between proband groups. Nonetheless, probands included in this study have nearly passed through the peak periods of risk for the development of both AN and most of the anxiety disorders (American Psychiatric Association, 1994). It is not unusual for the onset of some anxiety disorders, such as panic disorder, GAD, and PTSD, to occur much later in life, but it would be prohibitive to wait out such long risk periods prior to assessment of shared transmission. Moreover, participants in the present study were not a great deal younger than individuals included in other studies of comorbidity and transmission of eating and anxiety disorders (Braun et

al., 1994; Bulik et al., 1997; Deep et al., 1995; Halmi et al., 1991; Lilenfeld et al., 1998; Toner et al., 1988). Therefore, despite the young ages of probands, these results provide important initial data regarding comorbidity and transmission between disorders, and as such are important for understanding the development of eating and anxiety disorders.

References

Andrews, G., Stewart, G., Allen, R., & Henderson, A.S. (1990). The genetics of six neurotic disorders: A twin study. *Journal of Affective Disorders, 19*, 23-29.

American Psychiatric Association. (1994). *Diagnostic and statistical manual mental disorders (4th Ed.)*. Washington, DC: Author.

Beidel, D.C., & Turner, S.M. (1997). At risk for anxiety: I. Psychopathology in the offspring of anxious parents. *Journal of the Academy of Child and Adolescent Psychiatry, 36*, 918-924.

Bellodi, L., Cavallini, M.C., Bertelli, S., & Chiapparino, D. (2001). Morbidity risk for obsessive-compulsive spectrum disorders in first-degree relatives of patients with eating disorders. *The American Journal of Psychiatry, 158*, 563-569.

Braun, D.L., Sunday, S.R., & Halmi, K.A. (1994). Psychiatric comorbidity in patients with eating disorders. *Psychological Medicine, 24*, 859-867.

Brown, T.A. (1998). The relationship between obsessive-compulsive disorder and other anxiety-based disorders. In R. Swinson & M. Antony (Eds.), *Obsessive-Compulsive Disorder: Theory, research and Treatment* (pp. 207-226). New York, NY: The Guilford Press.

Bulik, C.M., Sullivan, P.F., Fear, J.L., & Joyce, P.R. (1997). Eating disorders and antecedent anxiety disorders: A controlled study. *Acta Psychiàtrica Scandinavica, 96*, 101-107.

Capps, L., Sigman, M., Sena, R., & Henker, B. (1996). Fear, anxiety and perceived control in children of agoraphobic parents. *Journal of Child Psychology and Psychiatry, 37*, 445-452.

Chatoor, I. (1999). Causes, symptoms, and effects of eating disorders: Child development as it relates to anorexia nervosa and bulimia nervosa. In R. Lemberg (Ed.) *Eating Disorders: A Reference Source Book* (pp. 17-21). Pheonix: The Oryx Press.

Deep, A.L., Nagy, L.M., Weltzin, T.E., Rao, R., & Kaye, W.H. (1995). Premorbid onset of psychopathology in long-term recovered anorexia nervosa. *International Journal of Eating Disorders, 17*, 291-297.

Fahy, T., Osacar, A., & Marks, I. (1993). History of eating disorders in female patients with obsessive-compulsive disorder. *International Journal of Eating Disorders, 14*, 439-443.

Fornari, V., Kaplan, M., Sandberg, D., Matthews, M., Skolnick, N., & Katz, J.L. (1992). Depressive and anxiety disorders in anorexia nervosa and bulimia nervosa. *International Journal of Eating Disorders, 12*, 21-29.

Galbaud du Fort, G., Newman, S.C., & Bland, R.C. (1993). Psychiatric comorbidity and treatment seeking. Sources of selection bias in the study of clinical populations. *The Journal of Nervous and Mental Disease, 181*, 467-474.

Garner, D.M., Garfinkel, P.E., Schwartz, D.M., & Thompson, M.M. (1980). Cultural expectations of thinness in women. *Psychological Reports, 47*, 483-491.

Garner, D.M., Olmstead, M.P., & Polivy, J. (1983). Development and validation of a multidimensional eating disorder inventory for anorexia nervosa and bulimia. *International Journal of Eating Disorders, 2*, 15-34.

Gershon, E.S., Hamovit, J.R., Schreiber, J.L., Dibble, E.D., Kaye, W., Nurnberger, J.I., et al. (1983). Anorexia nervosa and major affective disorders associated in families: A preliminary report. In S.B. Guze, F.J. Earls, & J.E. Barnett (Eds.), *Childhood Psychopathology and Development* (pp. 279-284) New York, NY: Raven Press.

Godart, N.T., Flament, M.F., Lecrubier, Y., & Jeammet, P. (2000). Anxiety disorders in anorexia nervosa and bulimia nervosa: Co-morbidity and chronology of appearance. *European Psychiatry, 15*, 38-45.

Godart, N.T., Flament, M.F., Perdereau, F., & Jeammet, P. (2001). Comorbidity between eating disorders and anxiety disorders: A review. *International Journal of Eating Disorders, 32*, 253-270.

Halmi, K.A., Eckert, E., Marchi, P., Sampugnaro, V., Apple, R., & Cohen, J. (1991). Comorbidity of psychiatric diagnoses in anorexia nervosa. *Archives of General Psychiatry, 48*, 712-718.

Herpertz-Dahlmann, B.M., Beate, M., Wewetzer, C., Schulz, E., Remschmidt, H. (1996). Course and outcome in adolescent anorexia nervosa. *International Journal of Eating Disorders, 19*, 335-345.

Herzog, D.B., Dorer, D.J., Keel, P.K., Selwyn, S.E, Ekeblad, E.R., Flores, A.T., et al. (1999). Recovery and relapse in anorexia and bulimia nervosa: A 7.5-year follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry, 38*, 829-837.

Herzog, D.B., Keller, M.B., Sacks, N.R., Yeh, C.J., & Lavori, P.W. (1992). Psychiatric comorbidity in treatment-seeking anorexics and bulimics. *Journal of the Academy of Child and Adolescent Psychiatry, 31*, 810-818.

Herzog, D.B., Nussbaum, K.M., & Marmor, A.K. (1996). Comorbidity and outcome in eating disorders. *The Psychiatric Clinics of North America, 19*, 843-859.

Hettema, J.M., Neale, M., & Kendler, K.S. (2001). A review and meta-analysis of the genetic epidemiology of anxiety disorders. *American Journal of Psychiatry, 158*, 1568-1578.

Hoek, H.W. (1993). Review of the epidemiological studies of eating disorders. *International Review of Psychiatry, 5*, 61-74.

Holland, A.J., Hall, A., Murray, R., Russell, G.F.M. & Crisp, A.H. (1984). Anorexia nervosa: A study of 34 twin pairs and one set of triplets. *British Journal of Psychiatry, 145*, 414-419.

Holland, A.J., Sicotte, J., & Treasure, J. (1988). Anorexia nervosa: Evidence for a genetic basis. *Journal of Psychosomatic Research, 32*, 561-571.

Hsu, L.K.G. (1990). *Eating disorders*. New York: Guilford Press.

Hudson, J.I., Harrison, G.P., Yurgelton-Todd, D., Jonas, J.M., & Frankenburg, F.R. (1987). A controlled study of lifetime prevalence of affective and other psychiatric disorders in bulimic outpatients. *American Journal of Psychiatry, 144*, 1283-1287.

Hudson, J.I., & Pope, H.G. (1990). Affective spectrum disorder: Does antidepressant response identify a family of disorders with a common pathophysiology? *American Journal of Psychiatry, 147*, 552-564.

Hudson, J.I., Pope, H.G., Jonas, J.M., & Yurgelton-Todd, D. (1983). Family history study of anorexia nervosa and bulimia. *British Journal of Psychiatry, 142*, 133-138.

Iacono, W.G., Carlson, S.R., Taylor, J., Elkins, I.J., & McGue, M. (1999). Behavioural disinhibition and the development of substance use disorders: findings from the Minnesota Twin Family Study. *Development and Psychopathology, 11*, 869-900.

Keel, P.K., Klump, K.L., Miller, K.B., McGue, M., & Iacono, W.G. (Manuscript submitted for publication). Shared transmission of eating disorders and comorbid disorders.

Kendler, K.S., Neale, M.C., Kessler, R.C., Heath, A.C., & Eaves, L.J. (1992). Major depression and generalized anxiety disorder: Same genes, (partly) different environments? *Archives of General Psychiatry, 49*, 716-722.

Kendler, K.S., Walters, E.E., Neale, M.C., Kessler, R.C., Heath, A.C., et al. (1995). The structure of the genetic and environmental risk factors for six major psychiatric disorders in women: Phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism. *Archives of General Psychiatry, 52*, 374-383.

Keys, A. (1948). Human starvation and its consequences. *Journal of the American Dietetic Association, 22*, 582-587.

Klump, K.L., McGue, M., & Iacono, W.G. (2000). Age difference in genetic and environmental influences on eating attitudes and behaviors in preadolescent and adolescent female twins. *Journal of Abnormal Psychology, 109*, 239-251.

Klump, K.L., McGue, M., & Iacono, W.G. (2003). Differential heritability of eating pathology in pre-pubertal versus pubertal twins. *International Journal of Eating Disorders, 33*, 287-292.

Klump, K.L., Miller, K.B., Keel, P.K., McGue, M., & Iacono, W.G. (2001). Genetic and environmental influences in a population-based twin sample. *Psychological Medicine, 31*, 737–740.

Kortegaard, L.S., Hoerder, K., Joergensen, J., Gillberg, C., & Kybik, K.O. (2001). A preliminary population-based twin study of self-reported eating disorder. *Psychological Medicine, 31*, 361-365.

Lilenfeld, L.R., Kaye, W.H., Greeno, C.G., Merikangas, K.R., Plotnicov, K., Pollice, C., et al. (1998). A controlled family study of anorexia nervosa and bulimia nervosa: Psychiatric disorders in first-degree relatives and effects of proband comorbidity. *Archives of General Psychiatry, 55*, 603-610.

Logue, C.M., Crowe, R.R., & Bean, J.A. (1989). A family study of anorexia nervosa and bulimia nervosa. *Comprehensive Psychiatry, 30*, 179-188.

Mancini, C., van Ameringen, M., Szatmari, P., Fugere, C., & Boyle, M. (1996). A high-risk pilot study of the children of adults with social phobia. *Journal of the Academy of Child and Adolescent Psychiatry, 35*, 1511-1517.

Metzger, R.L. (1976). A reliability and validity study of the State Trait Anxiety Inventory. *Journal of Clinical Psychology, 32*, 276-278.

Pasquale, L., Sciuto, G., Cocchi, S., Ronchi, P., & Bellodi, L. (1994). A family study of obsessive compulsive, eating and mood disorders. *European Psychiatry, 9*, 33-38.

Pollack, R.A., Carter, A.S., Avenevoli, S., Dierker, L.C., Chazan-Cohen, R. & Merikangas, K.R. (2002). Anxiety sensitivity in adolescents at risk for psychopathology. *Journal of Clinical Child and Adolescent Psychology, 31*, 343-353.

Pollice, C., Kaye, W., Greeno, C.G., & Weltzin, T.E. (1997). Relationship of depression, anxiety, and obsessionality to state of illness in anorexia nervosa. *International Journal of Eating Disorders, 21*, 367-376.

Reich, W., & Welner, Z. (1988). *Diagnostic Interview for Children and Adolescents – Revised: DSM-III-R version (DICA-R)*. St. Louis, MO: Washington University.

Rutherford, J., McGuffin, P., Katz, R.J., & Murray, R.M. (1993). Genetic influences on eating attitudes in a normal female twin population. *Psychological Medicine, 23*, 425-436.

Spielberger, C.D. (1983). *Manual for the State Trait Anxiety Inventory*. PaloAlto, CA: Consulting Psychologists Press.

Spielberger, C.D., Gonsuch, R., & Luschene, R. (1970). *Manual for the State Trait Anxiety Inventory (STAI)*. PaloAlto, CA: Consulting Psychologists Press.

Spitzer, R.L., Williams, J.B., & Gibbon, M. (1987). *Structured Clinical Interview for DSM-III-R (SCID)*. New York, NY: New York State Psychiatric Institute, Biometrics Research.

Stein, M.B., Jang, K.L., & Liveslety, W.J. (1999). Heriability of anxiety sensitivity: A twin study. *American Journal of Psychiatry, 156*, 246-251.

Strober, M., Freeman, R., Lampert, C., Diamond, J., & Kaye, W. (2000). Controlled family study of anorexia nervosa and bulimia nervosa: Evidence of shared liability and transmission of partial syndromes. *American Journal of Psychiatry, 157*, 393-401.

Strober, M., Freeman, R., & Morrell, W. (1997). The long-term course of severe anorexia nervosa in adolescents: Survival analysis of recovery, relapse, and outcome predictors over 10 -15 years in a prospective study. *International Journal of Eating Disorders, 22*, 339-360.

Strober, M., Lampert, C., Morrell, W., Burroughs, J., & Jacobs, C. (1990). A controlled family study of anorexia nervosa: Evidence of familial aggregation and lack of shared transmission with affective disorders. *International Journal of Eating Disorders, 9*, 239-253.

Strober, M., Morrell, W., Burroughts, J., Salkin, B., & Jacobs, C. (1985). A controlled family study of anorexia nervosa. *Journal of Psychiatric Research, 19*, 239-246.

Sullivan, P.F. (1995). Mortality in anorexia nervosa. *American Journal of Psychiatry, 152*, 1073-1074.

Toner, B., Garfinkel, P.E., & Garner, D.M. (1988). Affective and anxiety disorders in the long-term follow-up of anorexia nervosa. *International Journal of Psychiatry in Medicine, 18*, 357-364.

Torgersen, S. (1983). Genetic factors in anxiety disorders. *Archives of General Psychiatry, 40*, 1085-1089.

Turner, S.M., Beidel, D.C., & Costello, A. (1987). Psychopathology in the offspring of anxiety disorder patients. *Journal of Consulting and Clinical Psychology, 55*, 229-235.

von Eye, A. (1997). Prediction analysis program for 32 bit operation systems. *Methods of Psychological Research Online, 2*, http://www.pabst-publishers.de/mpr/.

von Ranson, K.M., Klump, K.L., Iacono, W.G., & McGue, M. (submitted). Development and validation of the Minnesota Eating Disorders Inventory: A brief measure of disordered eating attitudes and behaviours.

Wade, T.D., Bulik, C.M., Neale, M., & Kendler, K. (2000). Anorexia nervosa and major depression: Shared genetic and environmental risk factors. *American Journal of Psychiatry, 157*, 469-471.

Wade, T., Martin, N.G., Neale, M., Tiggeman, M., Treloar, S.A., Bucholz, K.K., Madden, P.A., & Heath, A.C. (1999). The structure of genetic and environmental risk factors for three measures of disordered eating. *Psychological Medicine, 4*, 925-934.

Walters, E.E., & Kendler, K.S. (1995). Anorexia nervosa and anorexic-like syndromes in a population-based female twin sample. *American Journal of Psychiatry, 152*, 64-71.

Weissman, M.M., Leckman, J.F., Merikangas, K.R., Gammon, G.D., & Prusoff, B.A. (1984). Depression and anxiety disorders in parents and children. *Archives of General Psychiatry, 41*, 845-852.

Wonderlich, S.A., & Mitchell, J.E. (1997). Eating disorders and comorbidity: Empirical, conceptual, and clinical implications. *Psychopharmacology Bulletin, 33*, 381-390.

Appendix

Table 1.

Lifetime rates of anxiety disorders among probands with anorexia nervosa and control probands without eating pathology.

Diagnosis in Probands	AN (n = 36)	Control (n = 287)	χ^2	p
Any anxiety disorder	17 (47.22%)	79 (27.53%)	5.94	0.02
Panic Disorder	2 (5.56%)	0	16.61	0.01
Agoraphobia	1 (2.78%)	0	8.56	0.11
Panic Disorder with Agoraphobia	0	0	---	---
Panic Disorder without Agoraphobia	2 (5.56%)	0	6.61	0.01
Agoraphobia without Panic Disorder	0	1 (0.35%)	.118	0.90
Specific Phobia	8 (22.22%)	32 (11.15%)	4.14	0.04
Social Phobia	5 (13.89%)	34 (11.85%)	.145	0.70
Generalized Anxiety Disorder	3 (8.33%)	2 (0.70%)	13.25	0.01
Post-Traumatic Stress Disorder	2 (5.56%)	3 (1.05%)	4.78	0.09
Separation Anxiety Disorder	2 (5.56%)	17 (5.92%)	.037	0.85
Overanxious Disorder	7 (19.44%)	24 (8.36%)	3.84	0.05

Table 2.

T-test comparing mean scores on State Trait Anxiety Inventory (STAI) subscales between probands with anorexia nervosa (AN) or no eating pathology (Controls).

STAI Subscale	AN (n = 35)	Controls (n = 278-279)	t	p
State	34.02 (8.71)	34.50 (8.00)	0.34 (312)	.74
Trait	37.83 (7.65)	37.74 (8.21)	-0.06 (311)	.95

Table 3

T-test comparing mean scores on State Trait Anxiety Inventory (STAI) subscales between probands with anorexia nervosa (AN), probands with anxiety, and probands with no eating or anxiety diagnoses (Controls).

STAI Subscale	A AN (n = 35)	B Anxiety (n = 78–79)	C Controls (n = 200)	F (df)	p	Contrast Results
State	34.02 (8.71)	37.41 (7.85)	33.36 (7.78)	7.49 (2)	.001	B > C
Trait	37.83 (7.65)	41.20 (8.55)	36.00 (7.41)	18.03 (2)	<.001	B > A, C

Table 4.

Rates of individual eating and anxiety disorders in parents of probands with AN, an anxiety disorder, or no eating or anxiety pathology (Controls).

Diagnosis	Parents of AN (n = 59)	Parents of Anxiety (n = 201)	Parents of Controls (n = 84-85)
Eating Disorders[a]			
AN	4 (6.78%)	0	0
BN	0	3 (1.49%)	0
BED	1 (1.69%)	7 (3.48%)	0
Anxiety Disorders			
PD	7 (11.86%)	12 (5.97%)	6 (7.06%)
Agoraphobia	6 (10.17%)	7 (3.48%)	3 (3.53%)
PD with agoraphobia	6 (10.17%)	6 (2.99%)	3 (3.53%)
PD without agoraphobia	1 (1.69%)	4 (1.99%)	3 (3.53%)
Agoraphobia without PD	1 (1.69%)	1 (0.50%)	0
Social Phobia	12 (20.34%)	41 (20.40%)	13 (15.29%)
Simple Phobia	17 (28.81%)	29 (14.43%)	8 (9.41%)
GAD	3 (5.08%)	4 (1.99%)	0

Note. AN = anorexia nervosa; BN = bulimia nervosa; BED = binge eating disorder; PD = panic disorder; GAD = generalized anxiety disorder.

[a]Fathers were not assessed for eating disorders.

Table 5.

Comparison of rates of eating disorders (ED), anxiety disorders, and no eating or anxiety pathology among parents of probands with anorexia nervosa (AN), an anxiety disorder, or no eating or anxiety pathology (Controls).

Diagnosis in Parents	Parents of AN (n = 59)	Parents of Anxiety (n = 201)	Parents of Controls (n = 85)
ED	5 (8.47%)	9 (4.48%)	0
Anxiety Disorder	28 (47.46%)	69 (34.33%)	24 (28.24%)
No eating or anxiety diagnoses	14 (23.73%)	60 (29.85%)	31 (36.47%)
Model Statistics			
Chi Square	$\chi^2 = 9.87$; df = 4; p = .04		
Prediction Analysis	z = 1.76; p = .04		
Odds Ratios			
Parents of probands with AN	OR_{ED}[a] = 9.38 (1.10 – 80.05)*		
	OR_{Anx} = 2.30 (1.14 – 4.60)*		
Parents of probands with anxiety	OR_{ED}[a] = 4.46 (0.56 – 35.36)		
	OR_{Anx} = 1.33 (0.76 – 2.31)		

Note. All odds ratios compared rates of disorders in the diagnostic group to those in the control group. 95% confidence intervals for the odds ratios are noted in parentheses.
[a]This odds ratio was calculated by adding 1 to each cell in order correct for cell values of 0.
* p<.05

Table 6.

ANOVA comparing M-EDI and STAI-Trait subscale means between parents of probands with anorexia nervosa (AN), an anxiety disorder, or no eating or anxiety pathology (Controls).

Scale	A Parents of AN (n = 55 - 57)	B Parents of Anxiety (n = 194 - 210)	C Parents of Controls (n = 78 - 82)	F (df)	p	Contrast Results
M-EDI total	7.63 (6.07)	6.55 (5.09)	5.06 (4.02)	4.68 (2)	0.01	A > C
BD	3.02 (2.48)	2.84 (2.30)	2.60 (2.32)	0.58 (2)	0.56	---
WP	2.26 (2.53)	1.89 (2.08)	1.20 (1.56)	5.21 (2)	0.01	A, B > C
CB	0.18 (0.38)	0.17 (0.47)	0.06 (0.29)	2.13 (2)	0.12	---
BE	1.68 (1.74)	1.20 (1.46)	0.88 (1.07)	5.35 (2)	0.01	A > C
STAI-T	37.32 (9.11)	34.81 (8.27)	32.95 (7.00)	4.66 (2)	0.01	A > C

Note. M-EDI = Minnesota Eating Disorders Inventory; BD = Body Dissatisfaction; WP = Weight Preoccupation; CB = Compensatory Behaviour; BE = Binge Eating; STAI-T = Trait subscale of the State-Trait Anxiety Inventory.

Table 7.

Comparison of rates of eating disorders (ED), anxiety disorders, and no eating or anxiety pathology among parents of probands with anorexia nervosa (AN) only, both AN and an anxiety disorder, one anxiety disorder, multiple anxiety disorders, or no eating or anxiety pathology.

Diagnosis in Parents	P of AN Only (n = 27)	P of AN+Anx (n = 32)	P of One Anx (n = 146)	P of Multi Anx (n = 55)	P of Controls (n = 85)
ED	1 (3.70%)	4 (12.50%)	5 (3.42%)	4 (7.27%)	0
AD	12 (44.44%)	16 (50.00%)	44 (30.14%)	25 (45.45%)	24 (28.24%)
No ED or Anx	7 (25.93%)	8 (25.00%)	48 (32.88%)	12 (21.82%)	31 (36.47%)
Model Statistics					
Chi Square			$\chi^2 = 16.86$; df = 8; p = 0.03		
Prediction Analysis			z = 1.76; p = 0.04		
Odds Ratios					
P of AN only			OR_{ED}[a] = 6.37 (0.56 – 73.02)		
			OR_{Anx} = 2.03 (0.83 – 4.97)		
P of AN+Anx			OR_{ED}[a] = 14.83 (1.66 – 132.21)*		
			OR_{Anx} = 2.54 (1.09 – 5.88)*		
P of One Anx			OR_{ED}[a] = 3.63 (0.43 – 30.70)		
			OR_{Anx} = 1.10 (0.61 – 1.98)		
P of Multi Anx			OR_{ED}[a] = 8.27 (0.94 – 72.75)		
			OR_{Anx} = 2.12 (1.05 – 4.31)*		

Note. Anx = anxiety disorder; AN+Anx = comorbid anorexia nervosa and an anxiety disorder; Multi Anx = more than one anxiety disorder; P = parents. All odds ratios compared rates of disorders in the diagnostic group to those in the control group. 95% confidence interval for the odds ratios are noted in parentheses.

[a] This odds ratio was calculated by adding 1 to each cell in order correct for cell values of 0.

Table 8.

ANOVA comparing M-EDI and STAI-T means between parents of probands with either anorexia nervosa (AN) only, AN and an anxiety disorder, an anxiety disorder, or no eating or anxiety pathology (Controls).

Scale	A Parents of AN only (n = 24-25)	B Parents of AN+Anx (n = 30-33)	C Parents of One Anx (n = 141- 156)	D Parents of Multiple Anx (n = 52 - 54)	E Parents of Controls (n = 78-82)	F (df)	p	Contrast Results
M-EDI total	7.67 (6.22)	7.61 (6.05)	6.03 (4.60)	7.90 (6.11)	5.06 (4.02)	3.67 (4)	0.01	D > E
BD	3.08 (2.50)	2.97 (2.51)	2.68 (2.26)	3.19 (2.36)	2.60 (2.32)	0.75 (4)	0.56	---
WP	2.25 (2.52)	2.27 (2.57)	1.78 (1.95)	2.21 (2.40)	1.20 (1.56)	3.03 (4)	0.02	D > E
CB	0.21 (0.41)	0.15 (0.36)	0.13 (0.40)	0.27 (0.63)	0.06 (0.29)	2.12 (4)	0.08	---
BE	1.67 (1.61)	1.70 (1.86)	1.04 (1.34)	1.62 (1.69)	0.88 (1.07)	4.25 (4)	0.00	B, D > E
STAI-T	34.83 (8.72)	39.40 (9.03)	33.90 (7.31)	37.46 (10.19)	32.95 (7.00)	5.48 (4)	0.00	B, D > E, C

Note. MEDI = Minnesota Eating Disorder Inventory; BD = Body Dissatisfaction; WP = Weight Preoccupation; CB = Compensatory Behaviour; BE = Binge Eating; STAI-T = Trait subscale of the State-Trait Anxiety Inventory.