Comorbidity of Anxiety Disorders With Anorexia and Bulimia Nervosa

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Objective: A large and well-characterized sample of individuals with anorexia nervosa and bulimia nervosa from the Price Foundation collaborative genetics study was used to determine the frequency of anxiety disorders and to understand how anxiety disorders are related to state of eating disorder illness and age at onset.

Method: Ninety-seven individuals with anorexia nervosa, 282 with bulimia nervosa, and 293 with anorexia nervosa and bulimia were given the Structured Clinical Interview for DSM-IV Axis I Disorders and standardized measures of anxiety, perfectionism, and obsessionality. Their ratings on these measures were compared with those of a nonclinical group of women in the community.

Results: The rates of most anxiety disorders were similar in all three subtypes of eating disorders. About two-thirds of the individuals with eating disorders had one or more lifetime anxiety disorder; the most common were obsessive-compulsive disorder (OCD) (N=277 [41%]) and social phobia (N=134 [20%]). A majority of the participants reported the onset of OCD, social phobia, specific phobia, and generalized anxiety disorder in childhood, before they developed an eating disorder. People with a history of an eating disorder who were not currently ill and never had a lifetime anxiety disorder diagnosis still tended to be anxious, perfectionistic, and harm avoidant. The presence of either an anxiety disorder or an eating disorder tended to exacerbate these symptoms.

Conclusions: The prevalence of anxiety disorders in general and OCD in particular was much higher in people with anorexia nervosa and bulimia nervosa than in a nonclinical group of women in the community. Anxiety disorders commonly had their onset in childhood before the onset of an eating disorder, supporting the possibility they are a vulnerability factor for developing anorexia nervosa or bulimia nervosa.

Clinical and epidemiological studies have consistently shown that the majority of people with anorexia nervosa or bulimia nervosa experience one or more anxiety disorders (1–3). Studies using trained interviewers and standardized diagnostic instruments in clinical samples have found that obsessive-compulsive disorder (OCD), social phobia, and specific phobia are the most common anxiety disorders in individuals with anorexia nervosa and bulimia nervosa. Other anxiety disorders, such as posttraumatic stress disorder (PTSD) and generalized anxiety disorder, appear to be less common; however, they were not routinely assessed in all studies.

Several studies have shown that, in most cases, the onset of anxiety disorders precedes the onset of anorexia nervosa or bulimia nervosa (4–6). Silberg and Bulik (7), using twins, identified a common genetic factor that influences liability to anxiety, depression, and eating disorder symptoms. This pattern of onset may simply reflect the natural course of the two disorders (i.e., the average age at onset of some anxiety disorders is younger than the average age at onset of anorexia nervosa), but it may also indicate that childhood anxiety represents one important genetically mediated pathway toward the development of anorexia nervosa and bulimia nervosa.

Despite this wealth of data, many questions regarding the nature of the relation between comorbid eating disorders and anxiety disorders remain unanswered (1). Most clinical studies have investigated relatively small groups of subjects with eating disorders and have lacked sufficient statistical power to characterize comorbidity patterns of the more uncommon anxiety disorders. In addition, few studies have been sufficiently large to subtype subjects with eating disorders accurately into clearly defined groups with anorexia nervosa, bulimia nervosa, or both anorexia and bulimia. To our knowledge, no study has compared patterns of comorbidity of anxiety disorders across these three well-defined diagnostic subcategories.

The Price Foundation has supported a multicenter, international collaborative study of the genetics of eating disorders. This study has included a collection of affected pairs consisting of probands with bulimia nervosa who have relatives with bulimia nervosa, anorexia nervosa, or a broad-spectrum eating disorder (8). The Price Foundation sample is sufficiently large and rigorously diagnosed to...
enable separation of participants into clearly defined eating disorder diagnostic subcategories.

The goals of the present study were to 1) calculate the frequency of all types of anxiety disorders in a large, well-characterized eating disorder sample; 2) understand how anxiety disorders are related to factors such as state of eating disorder illness and age at onset; and 3) compare temperament in subjects with eating disorders by lifetime anxiety disorders to determine whether personality phenotypes occur when anxiety disorders are controlled. We hope that these data will assist in identifying likely behavioral endophenotypes in our attempts to identify the genetic underpinnings of anorexia nervosa and bulimia nervosa.

Method

Collaborative Arrangements

This study was supported through funding provided by the Price Foundation under the principal direction of Walter H. Kaye of the University of Pittsburgh and Wade Berrettini of the University of Pennsylvania (see reference 8 for details). This initiative was developed through a cooperative arrangement among the Price Foundation, the University of Pittsburgh, and other academic sites in North America and Europe. The sites of collaborative arrangement, selected on the basis of experience in the assessment of eating disorders and geographical distribution, included the University of Pittsburgh, Cornell University, University of California at Los Angeles, University of Toronto, University of Munich, University of Pisa, University of North Dakota, University of Minnesota, and Harvard University. Each site obtained institutional review board approval separately from its own institution's human subjects committee.

Phenotypic Assessment

Proband met the following criteria: 1) DSM-IV lifetime diagnosis of bulimia nervosa, purging type; 2) age between 13 and 65 years; and 3) primarily of European descent. A current or lifetime history of anorexia nervosa was acceptable (some subjects had both bulimia nervosa and anorexia nervosa). (For further details see reference 8.)

Affected relatives were biologically related to the proband, were 13 to 65 years old, and had at least one of the following lifetime eating disorder diagnoses: 1) DSM-IV bulimia nervosa, purging type or nonpurging type; 2) DSM-IV anorexia nervosa, restricting type or binge eating/purging type (criteria were modified for this study to include individuals with and without amenorrhea); 3) or a subclinical eating disorder, defined as an eating disorder not otherwise specified. Affected relatives were excluded if they were a monozygotic twin of the proband, a biological parent with an eating disorder (unless there was another affected family member with whom the parent could be paired), or diagnosed with binge-eating disorder as their only lifetime eating disorder diagnosis.

Subjects were considered to be recovered if, for the last 12 months, they maintained normal weight and did not diet, restrict food intake, fast, binge-eat, purge, or exercise excessively. Cognitive components of an eating disorder, such as body image distortion and preoccupations with weight and shape, were not included in our definition because, for many individuals, these aspects persist, though often abated, long after weight restoration and cessation of eating disorder behaviors. Subjects were considered to be currently ill if they either met all diagnostic criteria or partial criteria for any eating disorder during the last 12 months.

Comparison Women From the Community

A comparison group of 694 healthy women were recruited by local advertisement and matched with the eating disorder subjects based on site, age range (except no comparison subjects under 18 years were included), ethnicity, and highest educational level completed. They were 18–65 years old, primarily of European ancestry, and at normal weight (lifetime body mass index range = 19–28). Comparison women were excluded if they had medical, psychiatric, or alcohol or drug disorders or a first-degree relative with an eating disorder. Psychiatric and substance exclusions were defined by the presence of any “likely” axis I disorder as assessed by the Structured Clinical Interview for DSM-IV (SCID) Screen Patient Questionnaire—Extended (9). Also excluded were women with a history of any substantial dieting, eating disorder behaviors, or excessive concerns with weight or shape, as defined by a score of 20 or higher on the Eating Attitudes Test-26 (10). Comparison women completed the same battery of self-report personality and symptom measures as probands and provided blood samples for genetic analysis.

Assessment Instruments

Assessment instruments are described in greater detail elsewhere (8). Eating disorder symptom profiles and diagnoses of probands and affected relatives were determined by using a modified version of the Structured Interview for Anorexic and Bulimic Disorders (11) and an expanded version of module H of the SCID (12). Lifetime major axis I anxiety disorder diagnoses were obtained by using the SCID; the Yale-Brown Obsessive Compulsive Scale (13) was administered in conjunction with the OCD section of the SCID. Anxiety disorder diagnoses were made according to DSM-IV criteria. We classified individuals who were one symptom short of the threshold diagnosis for anxiety disorders to have probable diagnoses. Both individuals with threshold diagnoses and those with probable diagnoses were included. The definitions for probable anxiety disorder are available on request (from Dr. Kaye). Participants completed the State-Trait Anxiety Inventory (14), the Frost Multidimensional Perfectionism Scale (15), and the Temperament and Character Inventory (16).

Statistical Methods

All statistical analyses were completed by using SAS 8.0 (SAS/STAT software, version 8. SAS Institute, Cary, N.C.). Logistic regression with the generalized estimating equation, which provides a chi-square value for testing significance, was used to correct for nonindependence of the sample caused by inclusion of family members and was applied to the data to compare rates of the different anxiety disorders across eating disorder subtypes. This same type of analysis was used to compare differences in patterns of onset of anxiety and eating disorders across the three eating disorder subgroups. In addition, a Poisson regression with a generalized estimating equation correction was completed to determine if there were differences in the number of anxiety disorders (defined as none, one, or more than one) among the eating disorder subgroups.

We used a two-step process to compare differences between currently ill and recovered participants with eating disorders who did or did not have a lifetime diagnosis of an anxiety disorder on different personality and anxiety scales. First, a linear regression was completed on each of the variables in question with body mass index and age as the regressors. The residuals from these analyses were then used to complete the regressions with the generalized estimating equation corrections to test for differences between the groups. The comparison women were then compared with subjects in the four eating disorder groups defined by eating disorder recovery status (recovered versus currently ill) and lifetime diagnosis of any anxiety disorder (present or absent) by using analysis of variance with generalized estimat-
ing equation corrections. However, because there were distribu-
tional differences between the comparison women and the
participants with eating disorders for most of the variables, non-
parametric statistical tests (PROC NPAR1WAY in SAS) were also
completed. Both methods yielded the same results. In addition,
effect sizes were calculated; an effect size exceeding 0.55, which
includes intermediate to large effects in the nomenclature of Co-
hen (17), was considered an indication of substantial differences.

Results

Prevalence of Anxiety Disorders

A total of 741 individuals with eating disorders were
given the SCID; 97 had anorexia nervosa, 282 had bulimia
nervosa, 293 had both anorexia and bulimia, and 69 had
an eating disorder not otherwise specified). Because of the
small number of individuals with an eating disorder not
otherwise specified and the diagnostic heterogeneity in-
herent in that subcategory, they were excluded from anal-
ysis, leaving a total of 672 participants. The vast majority
of individuals in each group were women (94 [96.9%] of
the subjects with anorexia nervosa, 278 [98.6%] of those
with bulimia nervosa, and 290 [99.0%] of those with anor-
exia and bulimia). Age did not differ across the three diag-
nostic groups; however, body mass index was significantly
lower for individuals in the group with anorexia nervosa
and the group with anorexia and bulimia than for the
group with bulimia nervosa. Of the entire sample, 427
(63.5%) were diagnosed with at least one anxiety dis-
order (Table 1). The most common anxiety disorder
was OCD, which occurred in approximately 40% of indi-
viduals, followed by social phobia (20%); other anxiety dis-
orders were somewhat less common.

Prevalence of Anxiety Disorders
by Eating Disorder Subtype

The prevalence of OCD, panic disorder, social phobia,
specific phobia, agoraphobia, and generalized anxiety dis-
order did not differ significantly across the three eating
disorder subtypes (Table 1). PTSD was significantly less
common among individuals with anorexia nervosa than
among those with bulimia nervosa and those with both
anorexia and bulimia. A nonsignificantly greater number
of individuals with anorexia nervosa than those with buli-
mia with or without anorexia had no lifetime anxiety dis-
orders (χ²=4.96, df=2, p=0.08) (data not included).
Age at Onset

Age at onset of the eating disorder was available for all participants. The age at onset of anxiety disorder was available for between 78% (specific phobia) and 98% (PTSD) of the individuals who had an anxiety disorder. If an individual stated that the anxiety disorder was present "as long as she or he could remember," we set the age at onset as 5 years old, assuming childhood recollections were limited before this age. For each eating disorder subtype, we determined whether the age at onset of the anxiety disorder was before or either concurrent with or subsequent to the onset of the eating disorder (Table 2). Eating disorder onset was defined as the age at which all of the symptoms necessary to make the diagnosis were present concurrently. Because there were no significant differences in patterns of onset of anxiety or eating disorder for any eating disorder subtype, the groups were combined. When all eating disorder subtypes were considered together, the onset of OCD, social phobia, specific phobia, and generalized anxiety disorder usually preceded the onset of the eating disorder. In contrast, PTSD, panic disorder, and agoraphobia most often developed after the onset of the eating disorder.

When the entire sample of individuals with eating disorders was considered, 23% had an onset of OCD, 13% had an onset of social phobia, and 10% had an onset of specific phobia in childhood, before the onset of an eating disorder (Table 2). Other anxiety disorders were less common. Overall, 282 (42%) of the entire sample had the onset of one or more anxiety disorders in childhood, before the onset of an eating disorder.

Relationship of Lifetime Anxiety Disorder and State of Eating Disorder Illness on Self-Report Assessments

Previous studies suggested that being ill with an eating disorder exacerbates anxiety-related symptoms in individuals with eating disorders (18). To determine how the state of the eating disorder was associated with anxiety symptoms, we compared individuals with eating disorders stratified by current illness state (currently ill versus symptom free for at least 12 months) (Table 3). In addition, to determine whether anxiety symptoms were present in the absence of an anxiety disorder diagnosis, we stratified participants by the presence versus absence of one or more lifetime anxiety disorder(s). Thus, the four cells for this analysis were characterized by current eating disorder and lifetime history of one or more anxiety disorders.

The four groups of eating disorder subjects were relatively similar in terms of age and weight. Age at the time of study differed significantly across the four groups, but the mean age span of the four groups was less than 5 years (high 20s to low 30s). Current body mass index was higher in the subjects without an anxiety disorder, regardless of state of eating disorder illness. However, body mass index differed by about one unit between groups. The four groups had similar ages at onset of their eating disorders.

In general, scores for anxiety, harm avoidance, perfectionism, and obsessionality tended to be highest in the individuals who had a lifetime anxiety disorder diagnosis and were ill with an eating disorder. Scores tended to be somewhat lower in those who either were currently ill with an eating disorder or had a lifetime anxiety disorder diag-

## TABLE 3. Demographic and Clinical Measures for Healthy Women in the Community and for Individuals With Remitted or Active Eating Disorders From the Price Foundation Collaborative Genetics Study Who Did or Did Not Have Lifetime Anxiety Disorders

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group 1 (N=82): Remitted Eating Disorder and No Anxiety Disorder</th>
<th>Group 2 (N=160): Active Eating Disorder and No Anxiety Disorder</th>
<th>Group 3 (N=111): Remitted Eating Disorder and One or More Anxiety Disorders</th>
<th>Group 4 (N=310): Active Eating Disorder and One or More Anxiety Disorders</th>
<th>Group 5 (N=694): Healthy Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset of eating disorder (years)</td>
<td>18.42 4.21</td>
<td>18.54 4.05</td>
<td>17.91 3.93</td>
<td>18.55 4.93</td>
<td>26.34 8.36</td>
</tr>
<tr>
<td>Age at time of study (years)</td>
<td>32.27 11.12</td>
<td>26.51 8.67</td>
<td>29.68 8.09</td>
<td>27.82 9.52</td>
<td>26.34 8.36</td>
</tr>
<tr>
<td>Body mass index at time of study</td>
<td>21.79 2.49</td>
<td>20.63 2.98</td>
<td>21.78 2.60</td>
<td>20.70 2.30</td>
<td>22.14 1.79</td>
</tr>
<tr>
<td>State-Trait Anxiety Inventory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait</td>
<td>35.29 10.44</td>
<td>42.32 12.62</td>
<td>40.96 12.19</td>
<td>50.53 13.77</td>
<td>27.14 6.63</td>
</tr>
<tr>
<td>State</td>
<td>38.65 10.44</td>
<td>45.75 12.57</td>
<td>45.47 11.57</td>
<td>54.20 12.91</td>
<td>29.44 6.92</td>
</tr>
<tr>
<td>Harm avoidance</td>
<td>13.79 5.61</td>
<td>17.33 7.28</td>
<td>19.06 7.29</td>
<td>21.50 7.34</td>
<td>10.83 5.39</td>
</tr>
<tr>
<td>Total perfectionism</td>
<td>83.39 24.15</td>
<td>85.81 22.39</td>
<td>94.67 22.92</td>
<td>96.73 23.64</td>
<td>60.53 15.89</td>
</tr>
<tr>
<td>Yale-Brown Obsessive Compulsive Scale</td>
<td>2.09 4.47</td>
<td>2.57 5.14</td>
<td>13.69 11.16</td>
<td>15.99 11.38</td>
<td></td>
</tr>
</tbody>
</table>

* Means and standard deviations were computed by using untransformed data.
* Differences with an effect size greater than 0.55, which includes intermediate to large effects, were considered substantial.
nosis. Individuals with eating disorders who had not been symptomatic with an eating disorder in the past 12 months and who never had a lifetime diagnosis of an anxiety disorder still had scores for anxiety, harm avoidance, and perfectionism that were significantly higher than those of the comparison women in the community. For subjects who were not currently ill with an eating disorder, the ratio of having no anxiety disorder to having an anxiety disorder was 0.74. In comparison, for people ill with an eating disorder, the ratio was 0.52 ($\chi^2$=3.85, df=1, p=0.05). Although this could reflect some bias in terms of recall, it may also suggest that not having an anxiety disorder has a modest association with recovery.

**Discussion**

To our knowledge, this study of 672 individuals with anorexia nervosa, bulimia nervosa, or anorexia and bulimia nervosa is the largest study to date to evaluate patterns of comorbidity of anxiety disorders and eating disorders and the only study to assess a wide range of anxiety disorders in rigorously defined subgroups of individuals with eating disorders. Overall, we observed that individuals with anorexia nervosa, bulimia nervosa, or anorexia and bulimia had relatively similar rates of all anxiety disorders, with the exception of PTSD, which was approximately three times more frequent in individuals with bulimia nervosa and those with anorexia and bulimia than in those with anorexia nervosa. In this sample, approximately two-thirds of participants with eating disorders reported one or more anxiety disorder in their lifetimes—the most common diagnoses were OCD (41%) and social phobia (20%). A substantial majority of the participants with eating disorders had the onset of OCD, social phobia, specific phobia, or generalized anxiety disorder in childhood, before the emergence of an eating disorder.

**Prevalence of Anxiety Disorders in Subgroups of Individuals With Eating Disorders**

Previous studies (1) have found elevated rates of anxiety disorders in individuals with eating disorders. However, these studies have assessed small groups of individuals, and many have used nonstructured or standardized instruments. Our study, which has three subgroups with rigorously defined subtypes of eating disorders (anorexia nervosa, bulimia nervosa, and anorexia and bulimia), showed that rates of most anxiety disorders were generally similar in these subgroups.

Aside from OCD, the rates of anxiety disorders in our study were usually within the range reported in a review of studies that used similar methods (1). In assessing OCD, we used the SCID and also incorporated information from the Yale-Brown Obsessive Compulsive Scale, which reviews a list of the most common obsessions and compulsions with the participant. The most frequently endorsed symptoms in individuals with eating disorders were symmetry, exactness, and order. It may be that people with eating disorders do not recognize these as OCD symptoms and consequently do not endorse the more general SCID screening probe. Thus, cases of OCD may be missed when the SCID is used alone.

The prevalence of PTSD was lower in the anorexia nervosa group than in the bulimia nervosa group and the anorexia and bulimia group. Although not significantly different, the prevalence of other anxiety disorders was also lower in the anorexia nervosa group. This could reflect an ascertainment bias: anorexia nervosa participants in this study were selected on the basis of being a relative of a proband with bulimia nervosa or anorexia and bulimia. Preliminary evidence from these studies suggests that overall severity of illness and comorbidity burden may be lower in individuals with anorexia nervosa who are included as affected relatives than in individuals who were ascertained as an anorexia nervosa proband.

**Comparison With Rates of Anxiety Disorders in Women in the Community**

Our study found that people with eating disorders had a 64% rate of lifetime anxiety disorders. This is clearly higher than the rates of 30.5% and 12.7%–18.1% for women in the community reported by Kessler et al. (19) and Wittchen and Essau (20), respectively. Similarly, the 41% frequency of OCD in people with eating disorders is much higher than the frequency found in community samples (in the low percents) (20, 21). Our study found that 20% of the individuals with eating disorders had social phobia. Kessler et al. (19) reported a rate of 15.5%, and Wittchen and Essau (20) reported a rate of 1%–3.5%. It is less certain whether
the rates for other anxiety disorders are higher than the rates for women in the community. That is because the rates for specific phobia, generalized anxiety disorder, panic disorder, and agoraphobia often have a wide range in community studies (19, 20).

**Onset of Anxiety Disorders Versus Onset of Eating Disorders**

Previous studies suggested that early-onset anxiety disorders represent a risk factor for the development of anorexia nervosa and bulimia nervosa in girls (4, 5, 7). Moreover, retrospective accounts of premorbid personality in children with anorexia nervosa often underscore pervasive anxiety as a dominant presentation (22, 23). This study showed that the onset of OCD, social phobia, specific phobia, and generalized anxiety disorder most commonly preceded the onset of an eating disorder. We calculated that 42% of the people with eating disorders in our total sample had the onset of one or more anxiety disorders in childhood. This is substantially higher than the frequency of overall anxiety disorders in childhood (4.7% to 17.7%) reported in 1995 (24). Most striking was the high rate of childhood-onset OCD (23%) in the subjects with eating disorders compared with community samples (2% to 3%) (25). This is all the more notable because the age of risk of the onset of OCD in women is often in the 20s. It is less certain whether people with eating disorders had elevated rates of childhood-onset social phobia (13% versus 0.6%–5.1% in community samples [24]), or of other anxiety disorders compared with community estimates (24).

**Relationship of Lifetime Anxiety Disorder and State of Eating Disorder Illness to Current Symptoms**

It has been reported (26–29) that people with eating disorders have more symptoms of anxiety, harm avoidance, obsessionality, and perfectionism, but it is less clear whether such symptoms are secondary to malnutrition and whether they persist after recovery. In general, we found that scores on measures of these symptoms tended to be most elevated in individuals who had a lifetime diagnosis of an anxiety disorder and were currently ill with an eating disorder. In comparison, scores tended to be lower in those with only one of these contributory factors. It is important to emphasize, however, that individuals who never had a lifetime anxiety disorder and who had been recovered from an eating disorder for at least 12 months still reported higher levels of anxiety, harm avoidance, and perfectionism than the healthy women in the community. This suggests that anxiety symptoms are traits present in most people with eating disorders, even if they do not meet DSM-IV criteria for anxiety disorders.

**Limitations**

First, we opted to report age at onset as the age at which all criteria for a full DSM eating disorder diagnosis were met, leading to an average age at onset of approximately 18 years. In some cases, individuals may have exhibited subthreshold eating disorder symptoms at younger ages. Second, age at onset of anxiety disorder diagnoses was not obtained for all individuals, either because they were unable to recall with confidence the age at onset or the question was not adequately assessed by the interviewer. Third, this study is subject to ascertainment bias; that is, our inclusion/exclusion criteria for the genetic study may have influenced the types of individuals who were selected for this study. Moreover, the fact that participants came from enriched pedigrees might have led to higher rates of comorbidity than would be seen in the community.

With these caveats in mind, these results both replicate previous studies of smaller and less well-characterized samples and extend our understanding of the nature of the relation between eating disorders and anxiety disorders and traits. We believe that genetic linkage analyses dependent solely on DSM-based phenotypes are unlikely to yield strong linkage signals for eating disorders; therefore, we have advocated the search for likely behavioral or temperamental endophenotypes to clarify the phenotypic definition of eating disorders. The present results underscore the pervasive presence of anxiety in individuals with eating disorders, even in the absence of frank anxiety disorders, and support further exploration of the biological and hence genetic relation between eating and anxiety pathology.
References
