Published in final edited form as:

Psychol Med. 2009 March ; 39(3): 451–461. doi:10.1017/S0033291708003826.

Anorexia nervosa trios: behavioral profiles of individuals with anorexia nervosa and their parents

M. J. Jacobs, S. Roesch, S. A. Wonderlich, R. Crosby, L. Thornton, D. E. Wilfley, W. H. Berrettini, H. Brandt, S. Crawford, M. M. Fichter, K. A. Halmi, C. Johnson, A. S. Kaplan, M. LaVia, J. E. Mitchell, A. Rotondo, M. Strober, D. B. Woodside, W. H. Kaye, and C. M. Bulik
University of California, San Diego (UCSD) Eating Disorders Treatment and Research Center, La Jolla, CA, USA

Abstract

Background—Anorexia nervosa (AN) is associated with behavioral traits that predate the onset of AN and persist after recovery. We identified patterns of behavioral traits in AN trios (proband plus two biological parents).

Method—A total of 433 complete trios were collected in the Price Foundation Genetic Study of AN using standardized instruments for eating disorder (ED) symptoms, anxiety, perfectionism, and temperament. We used latent profile analysis and ANOVA to identify and validate patterns of behavioral traits.

Results—We distinguished three classes with medium to large effect sizes by mothers' and probands' drive for thinness, body dissatisfaction, perfectionism, neuroticism, trait anxiety, and harm avoidance. Fathers did not differ significantly across classes. Classes were distinguished by degree of symptomatology rather than qualitative differences. Class 1 (~33 %) comprised low symptom probands and mothers with scores in the healthy range. Class 2 (~43 %) included probands with marked elevations in drive for thinness, body dissatisfaction, neuroticism, trait anxiety, and harm avoidance and mothers with mild anxious/perfectionistic traits. Class 3 (~24 %) included probands and mothers with elevations on ED and anxious/perfectionistic traits. Mother–daughter symptom severity was related in classes 1 and 3 only. Trio profiles did not differ significantly by proband clinical status or subtype.

Conclusions—A key finding is the importance of mother and daughter traits in the identification of temperament and personality patterns in families affected by AN. Mother–daughter pairs with severe ED and anxious/perfectionistic traits may represent a more homogeneous and familial variant of AN that could be of value in genetic studies.

Keywords

Anorexia nervosa; eating disorder; genetics; temperament

Introduction

A growing body of genetic research has associated anorexia nervosa (AN) with a cluster of behavioral traits that appear to predate onset of the disorder and persist following recovery (Fairburn et al. 1999; Price Foundation Collaborative Group, 2001; Devlin et al. 2002; Kaye

Correspondence to: M. J. Jacobs.

Declaration of Interest

None.

et al. 2003; Agras et al. 2004). These traits, which include perfectionism, anxiety and harm avoidance, may be susceptibility traits for developing AN and may also contribute to chronicity of illness and high relapse rates. In addition, these traits are heritable and occur in family members of individuals with AN (Jonnal et al. 2000; Kaye et al. 2004b; Tozzi et al. 2004). This is the first study to examine the patterns of behavioral traits in a large, carefully screened sample of AN probands and both of their biological parents.

The panel of traits chosen for this study comprises perfectionism, anxiety, and temperamental features, including novelty seeking and harm avoidance. Perfectionism has been identified as a potential risk factor for the development of AN (Fairburn et al. 1999; Halmi et al. 2000). Mothers of individuals with AN have shown evidence of elevated levels of perfectionism and drive for thinness relative to gender- and age-matched controls (Woodside et al. 2002). Anxiety has also been identified as a risk factor for AN. Anxiety disorders are more prevalent among individuals with AN than normal controls (Deep et al. 1995; Bulik et al. 1997; Kaye et al. 2004 a). Evidence suggests that anxious personality traits predate onset of AN and persist following recovery (Kaye et al. 2003). Individuals with AN often demonstrate low levels of novelty seeking and high levels of harm avoidance relative to controls (Fassino et al. 2002; Karwautz et al. 2003).

The personality characteristics described above may be present to a significant degree in AN families and create a temperamental susceptibility for AN (Sohlberg & Strober, 1994). Efforts to define eating disorder (ED) phenotypes empirically have motivated analyses based on behavioral traits rather than strictly diagnostic criteria (Goldner et al. 1999; Bulik et al. 2000, 2007; Westen & Harnden-Fischer, 2001; Keel et al. 2004). Although the literature suggests that differences in underlying behavioral traits may influence AN subtypes (i.e. restricting versus binge eating/purging), the precise nature of that relationship remains unclear (Herzog et al. 1996; Eddy et al. 2002; Ward et al. 2003; Vervaet et al. 2004). More recent longitudinal studies suggest that some of the previously identified differences between subtypes may reflect methodological issues (e.g. length of follow-up, sample size) rather than clear phenotypic differences (Herzog et al. 1996; Eddy et al. 2002). These methodological issues have clouded efforts to provide more definitive conclusions regarding the significance and/or appropriateness of the current taxonomy of AN (Herzog et al. 1996; Agras et al. 2004).

The primary aim of the present study was to identify cross-generational clusters of behavioral traits occurring among a large, rigorously screened sample of AN probands and their parents. We sought to characterize behavioral profiles of AN trios that could facilitate the identification of homogeneous and familial subtypes of AN that could be useful in genetic research. This is the first Price Foundation study to undertake such examination of parent-child trios. Our secondary aim included a validation of latent classes by comparing probands across latent classes on personality, clinical status, and ED subtype.

Method

Participants and study design

The sample for this analysis comprised individuals and parents enrolled in the multi-site International Price Foundation Study of the Genetics of Anorexia Nervosa (Kaye et al. 2000). This study is part of an effort to identify susceptibility loci for EDs. The sample of the present study includes 433 complete AN trios (proband plus two biological parents). An additional 88 probands had one participating parent; only probands with both participating parents were included in the trio analyses. In addition, because of the small number of males recruited into the study (n=12), only trios with female probands were included in the analyses. Participants with a history of AN were recruited from nine sites in Europe and the

USA, including: Pisa, Italy; Munich, Germany; Toronto, Canada; Fargo, ND; Pittsburgh, PA; New York, NY; Los Angeles, CA; Baltimore, MD; and Tulsa, OK, USA. Each participating site obtained approval from its local Institutional Review Board; all participants gave written informed consent to participate in the study.

Acceptance into the study did not require active illness at the time of assessment and was not restricted by sex of the proband. Current use of medication did not affect the eligibility of probands (Kaye et al. 2004 b). Probands entered into the study met the following criteria: (1) had an unequivocal lifetime diagnosis of AN [meeting modified DSM-IV criteria for AN (APA, 1994), excluding amenorrhea] at least 3 years prior to entry into the study; (2) low weight must have been less than the fifth percentile of body mass index (BMI) for age and gender on the Hebebrand (1996) chart of the National Health and Nutrition Examination Survey (NHANES) epidemiological sample (Hebebrand et al. 1996); (3) had an age of onset prior to age 25; (4) were Caucasian; and (5) were between the ages of 13 and 65 years. Subtypes were defined in the following manner: (1) restricting only (RAN), (2) purging with no binge eating (PAN), and (3) bingeing-purging subtype (BAN), which included individuals with binge eating with or without purging. The AN diagnosis is a lifetime diagnosis of AN and does not take into consideration other ED diagnoses. Probands could be currently ill or in remission at the time of study entry. Exclusionary criteria included onset of AN after age 25 or a lifetime history of any of the following: dementia; schizophrenia; mental retardation; organic brain syndrome; bipolar I or bipolar II, if symptoms of AN occurred only in the context of a manic or hypomanic episode; intelligence quotient (IQ) <70; maximum BMI since puberty >27 for females and >27.8 for males; medical condition affecting body weight, appetite, or eating behavior (i.e. individuals with diabetes and thyroid conditions were excluded if the onset of the disease preceded the onset of the ED). Parents of probands were invited to participate, regardless of age, medication status or psychiatric diagnosis. Parental participation was optional.

Measures

The assessment battery for this study was selected to facilitate ED diagnoses and to assess psychological and personality features that are known to be heritable and relevant to ED vulnerability. ED diagnoses and symptom profiles of probands were obtained using the Structured Inventory of Anorexia Nervosa and Bulimic Syndromes (SIAB; Fichter et al. 1998) and the expanded version of Module H of the Structured Clinical Interview of DSM-IV Axis I Disorders (SCID-I; First et al. 1996). The SIAB is a semi-structured clinical interview designed to obtain a detailed eating and weight history and to establish a DSM-IV ED diagnosis. ED recovery status and the presence or absence of ED behaviors (i.e. bingeing, purging) were obtained using the expanded version of Module H of SCID-I.

ED symptomatology of probands and parents was assessed using the Eating Disorder Inventory-2 (EDI-2; Garner, 1990), which is a 91-item questionnaire consisting of 11 subscales that assess specific cognitive and behavioral ED dimensions. The subscales included in the present study include the bulimia, drive for thinness, and body dissatisfaction subscales. The original version of the EDI (Garner et al. 1983) demonstrated good internal consistency, convergent and discriminant validity. The EDI has been widely used in ED research and is reported to successfully discriminate between subjects with and without EDs (Garner et al. 1983). The three subscales in the present study were chosen for their utility in assessing domains of primary interest.

Obsessions and compulsions of probands were assessed using the Yale-Brown Obsessive Compulsive Scale (YBOCS; Goodman et al. 1989) and the Yale-Brown-Cornell Eating Disorder Scale (YBC-EDS; Sunday et al. 1995). The YBOCS is a semi-structured interview designed to assess the presence and severity of obsessive thoughts and compulsive

behaviors. It has excellent inter-rater reliability and is considered to be the ‘gold standard’ for measuring OC symptom severity (Pato et al. 1994). The YBC-EDS is similar to the YBOCS, but assesses core obsessions and compulsions specific to EDs. The YBC-EDS has demonstrated excellent inter-rater reliability, internal consistency and convergent validity (Mazure et al. 1994).

Perfectionism in probands and parents was assessed using the Multidimensional Perfectionism Scale (MPS; Frost et al. 1990). The MPS is a 35-item factor-analytically developed questionnaire designed to evaluate overall perfectionism as well as six specific dimensions of perfectionism (including high personal standards, concern over mistakes, high perceived parental criticism, high perceived parental expectations, doubt about quality of performance, and need for organization, order, and precision). Internal consistency coefficients for the factor scales range from 0.77 to 0.93. The reliability of the overall perfectionism scale is 0.9 (Frost et al. 1990). The MPS has been shown to successfully discriminate between individuals with and without EDs (Srinivasagam et al. 1995). Supported by findings from Tozzi et al. (2004), the current study proceeded from the notion that perfectionism is a multi-dimensional construct. We used the MPS total score to best capture this multi-dimensionality. The Temperament and Character Inventory (TCI; Cloninger et al. 1993) was used to assess temperament in probands and parents. The TCI is a 240-item factor-analytically developed questionnaire measuring seven personality dimensions: four dimensions relate to temperament and three relate to character. The temperament dimensions include novelty-seeking, harm avoidance, reward dependence, and persistence. The character dimensions include self-directedness, cooperativeness, and self-transcendence. The TCI demonstrates acceptable internal consistency, ranging from 0.76 to 0.89 (Cloninger et al. 1994).

Neuroticism in probands and parents was measured using the Revised Neuroticism–Extroversion–Openness Personality Inventory (NEO PI-R; Costa & McCrae, 1992), which is a 240-item questionnaire that evaluates five major personality domains (neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness), based on the Five-Factor Model of personality. The subscale of interest in the present study was neuroticism, which is deemed to be a marker of psychopathology and psychological distress (Ormel et al. 2004). The neuroticism scale of the NEO PI-R measures the following six facets of the construct: anxiety, depression, angry hostility, impulsivity, self-consciousness, and vulnerability.

Impulsivity in probands and parents was assessed with the Barratt Impulsivity Scale-11 (BIS-11; Barratt, 1983), which is a 30-item self-report measure of impulsiveness. The BIS measures three aspects of impulsiveness: cognitive, motor, and non-planning. This measure has been shown to successfully discriminate the degree of impulse control in subgroups of women with eating disorders (Bulik et al. 1997).

Anxiety among probands and parents was assessed using the Spielberger State-Trait Anxiety Inventory (STAI; Spielberger et al. 1970), which is a widely used 40-item questionnaire that assesses current anxiety (state) and general levels of anxiety (trait). The questionnaire asks participants to report ‘how they feel at this moment’ and how they ‘generally feel’. State and trait assessments with this measure demonstrate high internal consistency, ranging from 0.86 to 0.96.

Statistical analysis

Latent profile analysis (LPA)—LPA was conducted to identify latent classes of trios with similar temperament and personality patterns. The rationale for using LPA in the present study was to use an empirically driven approach in defining clusters of trios based

on behavioral traits. LPA was performed using MPlus version 3.0 (Muthen & Muthen, 2004). The primary goals of LPA are to (a) identify the number of classes or groups that best represent the data (i.e. overall model fit) and (b) to substantively identify the classes. Model fit in the current study was determined using both the Vuong–Lo–Mendell–Rubin (VLMR) Likelihood Ratio test and the size-adjusted Bayesian information criteria (ABIC). The VLMR is a statistical test that compares a target class solution (e.g. 3) to a class solution that is fit with one fewer class (e.g. 2). A statistically significant result (i.e. $p < 0.05$) indicates that the higher class solution better represents the data. Once overall model fit is determined, substantive identification of classes is undertaken. To describe each class, the conditional response means for each indicator variable are evaluated. Each family member is treated as an independent entity in the analysis. All indicator variables were treated as conditionally independent.

The necessity of including data from three groups of participants, the large number of potential variables, and the limits on the number of variables that could meaningfully be examined in the LPA necessitated a parsimonious approach in choosing variables for inclusion. The variables included were those that have consistently demonstrated a relationship to the onset and maintenance of AN. To maximize the use of available data, key variables from several measures were chosen. As noted above, there is substantial support for the role of perfectionism, trait anxiety, harm avoidance, and neuroticism in AN, as well as drive for thinness and body dissatisfaction. Thus, these variables were chosen for inclusion in the trio analysis. The nature of LPA, which separates the three groups that have little within-group variability, obviated the need to include age as a covariate. Indicator variables included in the LPAs were the following: EDI drive for thinness and body dissatisfaction sub-scales; MPS total perfectionism score; NEO neuroticism subscale; STAI trait anxiety subscale; and TCI harm avoidance subscale.

Validation—To characterize the clusters, univariate ANOVA was conducted for the best-fitting class solution; ANOVA was used to identify significant differences between groups. Within-class differences were investigated using paired-sample *t* tests. External validation of the results of the LPAs was conducted to investigate whether classes derived from the LPAs demonstrated other clinically meaningful differences. Univariate ANOVA (with post-hoc comparisons) and χ^2 tests were used. Variables included in the external validation procedure included the following: EDI bulimia subscale; BIS motor, non-planning, and cognitive subscales; STAI state anxiety subscale; TCI novelty seeking and self-directedness subscales; YBC-EDS current total score (probands only); and YBOCS total score (probands only). The rationale for inclusion of these variables was based on a review of the literature establishing the relevance of these variables to domains being measured by the LPAs, including ED symptoms and characteristics related to temperament, anxiety and OC symptoms.

Because of the large number of comparisons, sample size and exploratory nature of many analyses included in this study, a conservative per comparison α -level of 0.001 was used to control for Type I error. Measures of effect size were also included.

Results

Demographics

Behavioral traits and demographic characteristics of participants in the present study are presented in Tables 1 and 2.

LPA

LPA indicated three distinct classes of families. The three-class solution had a VLMR significance level of $p=0.01$, indicating that the three-class solution was superior to a two-class solution; the three-class solution was also superior to a more complex, four-class solution. The ABIC for the three-class solution was 47365.9. In combination, the VLMR and the ABIC suggest that the three-class solution best fit the data. One class, constituting approximately 33% of the sample, reported less extreme scores than classes 2 (~43 % of the sample) and 3 (~24 % of the sample) on the vast majority of variables that significantly differed between classes (see Tables 3 and 4). The three classes will be referred to using the following labels: moderate symptomatology probands/healthy mothers (class 1), highest symptomatology probands/moderate symptomatology mothers (class 2), and high symptomatology probands/high symptomatology mothers (class 3). Fathers in the three classes did not differ significantly on any of the variables tested.

One-way ANOVA was conducted for each variable that differed significantly between classes of families, followed by pairwise comparisons to further explore significant differences between groups. Detailed findings for each subgroup and variable investigated are available in the accompanying tables (Tables 3 and 4). Class 1 was characterized by probands with moderate levels of symptoms compared to the other probands and low symptom mothers. With the exception of maternal perfectionism, this group reported the lowest levels of both proband and mother drive for thinness, body dissatisfaction, neuroticism, trait anxiety, harm avoidance, and proband perfectionism.

For the most part, class 2 was characterized by the highest levels of symptoms among probands and mothers with moderate symptoms relative to mothers in the other two classes. Finally, class 3 was characterized by having both probands and mothers with high levels of symptoms relative to the other classes on many of the variables investigated. More specifically, the mothers in this class had the highest levels of drive for thinness, body dissatisfaction, perfectionism, neuroticism, and harm avoidance relative to mothers in the other classes. Probands in this class reported greater symptomatology than class 1 probands but less than class 2 probands.

Comparisons between mothers and daughters within latent classes indicated that mothers and daughters in two of the classes (classes 1 and 2) differed significantly from each other within clusters ($p<0.001$). More specifically, within classes 1 and 2, mothers and daughters differed significantly from each other on neuroticism, trait anxiety, and harm avoidance, as well as drive for thinness, body dissatisfaction, and perfectionism. Within class 3, however, mothers and daughters differed significantly from each other only on drive for thinness, body dissatisfaction, and perfectionism ($p<0.001$). The class 3 mothers and daughters did not differ significantly from each other on neuroticism, trait anxiety, or harm avoidance.

Validation of classes

χ^2 tests conducted to investigate whether AN subtype or clinical status was related to family class membership indicated that class membership was not significantly related to probands' illness subtype [$\chi^2(4)=6.18$, $p=0.186$, Cramer's $V=0.09$] or clinical status [$\chi^2(2)=2.75$, $p=0.253$, Cramer's $V=0.09$]. The moderate symptomatology probands/healthy mothers class (class 1) was composed of 55.8% RAN probands, 17.5 % PAN and 26.7 % BAN. The highest symptomatology probands/moderate symptomatology mothers class (class 2) was composed of 67.7% RAN probands, 14.6 % PAN, and 17.7 % BAN. The high symptomatology probands/high symptomatology mothers class (class 3) was composed of 58.6% RAN probands, 21.8% PAN and 19.6% BAN.

In the external validation, one-way ANOVAS with post-hoc comparisons were conducted. There were no significant differences between groups at the $\alpha=0.001$ level (see Table 5). The proband current YBC-EDS total score indicated a trend toward significance [$F(2, 362)=4.55$, $p=0.011$, $g^2=0.03$], with class 3 probands reporting the highest scores on this variable (mean=15.99, S.D.=8.30).

Discussion

This study of temperament and personality characteristics of AN probands and their parents identified distinct patterns of traits within AN families. The three distinct classes of trios were distinguished by levels of symptoms on selected variables rather than qualitative pattern differences.

The first class of trios contained probands and mothers with the least symptomatology. The patterns of scores within the other two classes of trios were characterized by counterbalancing scores for mothers and probands. In the second class of trios (highest symptomatology probands/moderate symptomatology mothers), mothers with mid-range scores had daughters with the highest proband scores. The mothers in this class reported lower levels of perfectionism and drive for thinness than AN mothers in the other trio classes, although elevated compared to the healthy comparison women (Woodside et al. 2002). Significant differences between mothers and daughters on all variables within this class confirm the more severe symptomatology of the probands.

Mothers with the highest scores on the trio LPA variables had daughters with mid-range scores relative to other probands. It should be noted that the probands' raw scores on a majority of variables were higher than their mothers' scores. Probands in this class demonstrated higher levels of symptomatology than the least symptomatic probands (moderate symptomatology probands/healthy mothers, class 1) and their own mothers. Unlike the other trio classes, however, mothers and daughters in the high symptomatology probands/high symptomatology mothers class did not significantly differ on all variables in the LPA. More specifically, they did not differ significantly with respect to neuroticism, harm avoidance, and trait anxiety. Thus, these mothers demonstrated levels of personality, temperamental, and affective disturbance in the same range as their daughters. The significantly higher perfectionism of the probands compared to their mothers provides support for the notion that perfectionism may moderate the relationship between personality, temperamental, and affective disturbances and the development and maintenance of AN.

Taken together, the results of the trios LPA indicate differences in severity in both probands and mothers across the classes, rather than qualitative pattern differences. The more severe symptomatology of two of the classes [the highest symptomatology probands/moderate symptomatology mothers (class 2) and the high symptomatology probands/high symptomatology mothers (class 3)] is consistent with the pervasive temperamental and behavioral disturbances that have been identified previously in AN (Agras et al. 2004). Consistent with our findings, a small study examining temperament and character in AN daughters and parents found selected positive correlations between daughters and mothers, but not between daughters and fathers (Fassino et al. 2002). No larger, more comparable studies could be identified. The finding that more temperamentally healthy mothers tended to have daughters with less severe temperamental symptomatology relative to other probands suggests that these daughters may benefit from a different genetic loading for these characteristics than more highly symptomatic probands. When reflecting on the mechanism whereby genetics might influence risk for a complex trait such as AN, we envision the action of many genes across risk domains including appetite, weight regulation, and temperament. These results indicate that 'healthier' mothers were not associated with

offspring with high severity of ED symptomatology. It is conceivable that more extreme temperamental traits (in both probands and their mothers) may influence severity of symptoms expressed. We hypothesize that the transmission of milder temperamental profiles may protect offspring from developing more severe AN symptomatology. This could reflect the direct genetic transmission of milder temperamental traits, or could index the family environment influenced by mothers with milder temperaments, environments that may serve to contain the expression of AN symptoms rather than exacerbate them.

The risk factors for the development of EDs are poorly understood. Findings in this study using LPA to identify temperamental, personality, and affective disturbances among family members are consistent with previous reports from other Price Foundation studies (Lilenfeld et al. 1998; Woodside et al. 2002; Keel et al. 2004) as well as other studies (Fairburn et al. 1999; Espina, 2003) noting familial personality profiles in AN. In this study, class membership was more strongly influenced by maternal and proband characteristics. It is possible that other factors not captured in this study, such as inflexibility and rigidity, may be related to fathers (Lilenfeld et al. 1998). Perhaps the assessment battery (which did not assess OC symptoms in parents) failed to capture dimensions that are characteristic of fathers of individuals with AN.

Although neuroticism, trait anxiety, and harm avoidance contributed the most to the determination of class groups, mothers and daughters within classes 1 and 2 differed significantly on these variables. Given the considerable genetic contribution thought to be associated with these traits (Cloninger et al. 1993; Jang et al. 1996; Price Foundation Collaborative Group, 2001; Fassino et al. 2002), it may initially seem counterintuitive that mothers and daughters within two classes differed significantly on these traits. It may be that the higher levels of severity among daughters (relative to mothers) reflects the impact of lifetime eating disordered behavior or may have driven that behavior initially. In addition, there may be traits that were not assessed that help to explain the mismatch. We are just starting to understand the biology of AN and it is not possible to understand or include all potentially relevant factors.

Contrary to the initial hypotheses, the differences in personality and temperament patterns among the trio classes were not related to subtype or clinical status. Potential implications are that differences in subtype may not be related to family temperament and personality profiles and that profiles are stable to clinical status. It is possible, however, that subtype results were influenced by an under-representation of AN probands with binge eating. The resulting latent classes, distinguished by symptom levels rather than by qualitatively distinct patterns, could reflect the relative diagnostic homogeneity of the probands. We would like to emphasize, however, that if a subtype were truly homogeneous, this would be reflected in the LPA results. Under-representation would only seriously threaten the validity of the LPA at about 5 % representation. The selection of indicator variables could also have influenced the resultant latent classes. For example, including the EDI-2 bulimia subscale as an indicator variable in the LPA (instead of in the external validation) could have potentially produced different class groupings. Nevertheless, it is not likely that this would threaten the null finding with respect to subtype, given that there were no significant differences between classes on the bulimia subscale in the external validation.

Although no significant differences in trio class membership were identified based on OC symptoms of the probands, it should be noted that all three classes of trios reported elevated OC symptoms relative to controls (Kaye et al. 1992; Rosenfeld et al. 1992; Sunday & Halmi, 2000). This may indicate a ceiling effect and is consistent with literature highlighting the important role of OC symptoms in the etiology (Lilenfeld et al. 1998) and course of AN (Keel et al. 2004).

The strengths of the present study include the large sample size, comprehensive assessment protocol, diagnostic homogeneity of the probands, and inclusion of both biological parents of individuals with AN. Nevertheless, families included may differ systematically from families in which both parents were not available and/or willing to participate. Other potential sources of variance, particularly related to the inclusion of relatives who may have had other Axis I psychiatric diagnoses (Kaye et al. 2004 b) or the possible presence of parents with a lifetime ED diagnosis, must be acknowledged. History of an ED may help to explain the role of mothers compared to fathers in determining class profiles. Risk factors for EDs are not well understood and variables not captured by the assessment battery in this study, including past parental ED, may contribute to an enhanced understanding of its findings (Jacobi et al. 2004). Finally, this study does not contain an unaffected comparison group of trios. Similar profiles of trios may exist within the unaffected population. Nevertheless, exploring differences within the affected sample may help us to better understand diversity within the ED population and to explore genetic variants and commonalities.

A key finding of this study is the importance of mothers' and daughters' traits relative to fathers' in the identification of temperament and personality patterns in families affected by AN. The high symptomatology probands/high symptomatology mothers class (class 3) may represent a more homogeneous and familial variant of AN and index an underlying anxiety/harm avoidant dimension and/or propensity to extreme fear conditioning hypothesized to be related to AN (Strober, 2004). Identification of phenotypes that evidence strong familiarity can assist with choosing optimal quantitative traits for inclusion in linkage and association studies.

Acknowledgments

We thank the Price Foundation for support in the clinical collection of participants and in data analysis. We thank the staff of the Price Foundation Collaborative Group for their efforts in participant screening and clinical assessments. We are indebted to the participating families for their contribution of time and effort in support of this study.

References

- Agras WS, Brandt HA, Bulik CM, Dolan-Sewell R, Fairburn CG, Halmi KA, Herzog DB, Jimerson DC, Kaplan AS, Kaye WH, Le Grange D, Lock J, Mitchell JE, Rudorfer MV, Street LL, Striegel-Moore R, Vitousek KM, Walsh BT, Wilfley DE. Report of the National Institutes of Health workshop on overcoming barriers to treatment research in anorexia nervosa. *International Journal of Eating Disorders*. 2004; 35:509–521. [PubMed: 15101067]
- APA. *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association; Washington, DC: 1994.
- Barratt ES. The biological basis of impulsiveness: the significance of timing and rhythm. *Personality and Individual Differences*. 1983; 4:387–391.
- Bulik CM, Hebebrand J, Keski-Rahkonen A, Klump KL, Mazzeo SE, Reichborn-Kjennerud T, Wade TD. Genetic epidemiology, endophenotypes, and eating disorder classification. *International Journal of Eating Disorders*. 2007; 40 (Suppl):S52–S60. [PubMed: 17573683]
- Bulik CM, Sullivan PF, Fear JL, Joyce PR. Eating disorders and antecedent anxiety disorders: a controlled study. *Acta Psychiatrica Scandinavica*. 1997; 96:101–107. [PubMed: 9272193]
- Bulik CM, Sullivan PF, Kendler KS. An empirical study of the classification of eating disorders. *American Journal of Psychiatry*. 2000; 157:886–895. [PubMed: 10831467]
- Cloninger, CR.; Przybeck, TR.; Svrakic, DM.; Wetzell, RD. *The Temperament and Character Inventory (TCI): A Guide to its Development and Use*. Center for Psychobiology of Personality: Washington University; St Louis, MO: 1994.

- Cloninger CR, Svrakic DM, Przybeck TR. A psychobiological model of temperament and character. *Archives of General Psychiatry*. 1993; 50:975–990. [PubMed: 8250684]
- Costa, PT.; McCrae, RR. NEO PI-R Professional Manual. Psychological Assessment Resources; Odessa, FL: 1992.
- Deep AL, Nagy LM, Weltzin TE, Rao R, Kaye WH. Premorbid onset of psychopathology in long-term recovered anorexia nervosa. *International Journal of Eating Disorders*. 1995; 17:291–297. [PubMed: 7773266]
- Devlin B, Bacanu SA, Klump KL, Bulik CM, Fichter MM, Halmi KA, Kaplan AS, Strober M, Treasure J, Woodside DB, Berrettini WH, Kaye WH. Linkage analysis of anorexia nervosa incorporating behavioral covariates. *Human Molecular Genetics*. 2002; 11:689–696. [PubMed: 11912184]
- Eddy KT, Keel PK, Dorer DJ, Delinsky SS, Franko DL, Herzog DB. Longitudinal comparison of anorexia nervosa subtypes. *International Journal of Eating Disorders*. 2002; 31:191–201. [PubMed: 11920980]
- Espina A. Alexithymia in parents of daughters with eating disorders: its relationships with psychopathological and personality variables. *Journal of Psychosomatic Research*. 2003; 55:553–560. [PubMed: 14642987]
- Fairburn C, Cooper Z, Doll H, Welch S. Risk factors for anorexia nervosa: three integrated case-control comparisons. *Archives of General Psychiatry*. 1999; 56:468–476. [PubMed: 10232302]
- Fassino S, Svrakic D, Abbate-Daga G, Leombruni P, Amianto F, Stanic S, Rovera GG. Anorectic family dynamics: temperament and character data. *Comprehensive Psychiatry*. 2002; 43:114–120. [PubMed: 11893989]
- Fichter MM, Herpetz S, Quadflieg N, Herpetz-Dahlmann B. Structured interview for anorexic and bulimic disorders for DSM-IV and ICD-10: updated (third) revision. *International Journal of Eating Disorders*. 1998; 24:227–249. [PubMed: 9741034]
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JB. Biometrics Research Department. New York State Psychiatric Institute; New York: 1996. Structured Clinical Interview for Axis I DSM-IV Disorders.
- Frost RO, Marten P, Lahart C, Rosenblate R. The dimensions of perfectionism. *Cognitive Therapy and Research*. 1990; 14:449–468.
- Garner, DM. Eating Disorder Inventory-2 Professional Manual. Psychological Assessment Resources; Odessa, FL: 1990.
- Garner DM, Olmsted MP, Polivy J. Development and validation of a multidimensionaleating disorder inventory for anorexia and bulimia nervosa. *International Journal of Eating Disorders*. 1983; 2:15–34.
- Goldner EM, Srikameswaran S, Schroeder ML, Livesley WJ, Birmingham CL. Dimensional assessment of personality pathology in patients with eating disorders. *Psychiatry Research*. 1999; 85:151–159. [PubMed: 10220006]
- Goodman WH, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, Heninger GR, Chamey DS. The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS): I. Development, use, and reliability. *Archives of General Psychiatry*. 1989; 46:1006–1011. [PubMed: 2684084]
- Halmi KA, Sunday SR, Strober M, Kaplan A, Woodside DB, Fichter M, Treasure J, Berrettini WH, Kaye WH. Perfectionism in anorexia nervosa: variation by clinical subtype, obsessiveness, and pathological eating behavior. *American Journal of Psychiatry*. 2000; 157:1799–1805. [PubMed: 11058477]
- Hebebrand J, Himmelmann GW, Hesecker H, Schafer H, Remschmidt H. Use of percentiles for the body mass index in anorexia nervosa: diagnostic, epidemiological, and therapeutic considerations. *International Journal of Eating Disorders*. 1996; 19:359–369. [PubMed: 9156689]
- Herzog DB, Field AE, Keller MB, West JC, Robbins WM, Staley J, Colditz GA. Subtyping eating disorders: is it justified ? *Journal of the American Academy of Child and Adolescent Psychiatry*. 1996; 35:928–936. [PubMed: 8768354]
- Jacobi C, Hayward C, de Zwaan M, Kraemer HC, Agras WS. Coming to terms with risk factors for eating disorders: application of risk terminology and suggestions for a general taxonomy. *Psychological Bulletin*. 2004; 130:19–65. [PubMed: 14717649]

- Jang KL, Livesley WJ, Vernon PA. Heritability of the big five personality dimensions and their facets: a twin study. *Journal of Personality*. 1996; 64:577–591. [PubMed: 8776880]
- Jonnal AH, Gardner CO, Prescott CA, Kendler KS. Obsessive and compulsive symptoms in a general population sample of female twins. *American Journal of Medical Genetics*. 2000; 96:791–796. [PubMed: 11121183]
- Karwautz A, Troop NA, Rabe-Hesketh S, Collier DA, Treasure JL. Personality disorders and personality dimensions in anorexia nervosa. *Journal of Personality Disorders*. 2003; 17:73–85. [PubMed: 12659548]
- Kaye WH, Barbarich NC, Putnam K, Gendall KA, Fernstrom J, Fernstrom M, McConaha CW, Kishore A. Anxiolytic effects of acute tryptophan depletion in anorexia nervosa. *International Journal of Eating Disorders*. 2003; 33:257–267. [PubMed: 12655621]
- Kaye WH, Bulik CM, Thornton L, Barbarich N, Masters K, Group PFC. Comorbidity of anxiety disorders with anorexia and bulimia nervosa. *American Journal of Psychiatry*. 2004a; 161:2215–2221. [PubMed: 15569892]
- Kaye WH, Devlin B, Barbarich N, Bulik CM, Thornton L, Bacanu SA, Fichter MM, Halmi KA, Kaplan AS, Strober M, Woodside DB, Bergen AW, Crow S, Mitchell J, Rotondo A, Mauri M, Cassano G, Keel P, Plotnicov K, Pollice C, Klump K, Lilienfeld LR, Ganjei JK, Quadflieg N, Berrettini WH. Genetic analysis of bulimia nervosa: methods and sample description. *International Journal of Eating Disorders*. 2004b; 35:556–570. [PubMed: 15101071]
- Kaye WH, Lilienfeld LR, Berrettini WH, Strober M, Devlin B, Klump KL, Goldman D, Bulik CM, Halmi KA, Fichter MM, Kaplan A, Woodside DB, Treasure J, Plotnicov KH, Pollice C, Rao R, McConaha CW. A search for susceptibility loci for anorexia nervosa: methods and sample description. *Biological Psychiatry*. 2000; 47:794–803. [PubMed: 10812038]
- Kaye WH, Weltzin TE, Hsu LKG, Bulik C, McConaha C, Sobkiewicz T. Patients with anorexia nervosa have elevated scores on the Yale-Brown Obsessive Compulsive Scale. *International Journal of Eating Disorders*. 1992; 12:57–62.
- Keel PK, Fichter M, Quadflieg N, Bulik CM, Baxter MG, Thornton L, Halmi KA, Kaplan AS, Strober M, Woodside DB, Crow SJ, Mitchell JE, Rotondo A, Mauri M, Cassano G, Treasure J, Goldman D, Berrettini WH, Kaye WH. Application of a latent class analysis to empirically define eating disorder phenotypes. *Archives of General Psychiatry*. 2004; 61:192–200. [PubMed: 14757596]
- Lilienfeld LR, Kaye WH, Greeno CG, Merikangas KR, Plotnicov K, Pollice C, Rao R, Strober M, Bulik C, Nagy L. A controlled family study of anorexia nervosa and bulimia nervosa. *Archives of General Psychiatry*. 1998; 55:603–610. [PubMed: 9672050]
- Mazure CM, Halmi KA, Sunday SR, Romano SJ, Einhorn AM. The Yale-Brown-Cornell Eating Disorder Scale: development, use, reliability, and validity. *Journal of Psychiatric Research*. 1994; 28:425–445. [PubMed: 7897615]
- Muthen, BO.; Muthen, LK. *Mplus User's Guide, Version 3*. Muthen & Muthen; Los Angeles: 2004.
- Ormel J, Rosmalen J, Farmer A. Neuroticism: a non-informative marker of vulnerability to psychopathology. *Social Psychiatry and Psychiatric Epidemiology*. 2004; 39:906–912. [PubMed: 15549243]
- Pato, MT.; Eisen, J.; Pato, CN. Rating scales for obsessive compulsive behavior. In: Hollander, E.; Zohar, J.; Marassati, D.; Olivier, B., editors. *Current Insights in Obsessive Compulsive Disorder*. John Wiley & Sons; New York: 1994. p. 77-91.
- Price Foundation Collaborative Group. Deriving behavioral phenotypes in an international, multi-centre study of eating disorders. *Psychological Medicine*. 2001; 31:635–645. [PubMed: 11352366]
- Rosenfeld R, Reuven D, Anderson D, Kobak KA, Greist JH. A computer-administered version of the Yale-Brown Obsessive-Compulsive Scale. *Psychological Assessment*. 1992; 4:329–332.
- Sohlberg S, Strober M. Personality in anorexia nervosa: an update and a theoretical integration. *Acta Psychiatrica Scandinavica*. 1994; 378:1–15. [PubMed: 8209696]
- Spielberger, CD.; Gorsuch, RL.; Lushene, RE. *STAI Manual for the Stait Trait Personality Inventory*. Consulting Psychologists Press; Palo Alto: 1970.
- Srinivasagam NM, Plotnicov KH, Greeno CG, Weltzin TE, Rao R, Kaye WH. Persistent perfectionism, symmetry, and exactness in anorexia nervosa after long-term recovery. *American Journal of Psychiatry*. 1995; 152:1630–1634. [PubMed: 7485626]

- Strober M. Pathologic fear conditioning and anorexia nervosa: on the search for novel paradigms. *International Journal of Eating Disorders*. 2004; 35:504–508. [PubMed: 15101066]
- Sunday SR, Halmi K. Comparison of the Yale-Brown-Cornell Eating Disorders Scale in recovered eating disorder patients, restrained dieters, and nondieting controls. *International Journal of Eating Disorders*. 2000; 28:455–459. [PubMed: 11054794]
- Sunday SR, Halmi KA, Einhorn A. The Yale-Brown-Cornell Eating Disorder Scale: a new scale to assess eating disorder symptomatology. *International Journal of Eating Disorders*. 1995; 18:237–245. [PubMed: 8556019]
- Tozzi F, Aggen SH, Neale BM, Anderson CB, Mazzeo SE, Neale MC, Bulik CM. The structure of perfectionism: a twin study. *Behavior Genetics*. 2004; 34:483–494. [PubMed: 15319571]
- Vervaeke M, van Heeringen C, Audenaert K. Personality-related characteristics in restricting versus bingeing and purging eating disorders. *Comprehensive Psychiatry*. 2004; 45:37–43. [PubMed: 14671735]
- Ward A, Campbell IC, Brown N, Treasure J. Anorexia nervosa subtypes: differences in recovery. *Journal of Nervous and Mental Disease*. 2003; 191:197–201. [PubMed: 12637848]
- Westen D, Harnden-Fischer J. Personality profiles in eating disorders: rethinking the distinction between Axis I and Axis II. *American Journal of Psychiatry*. 2001; 158:547–562. [PubMed: 11282688]
- Woodside DB, Bulik CM, Halmi KA, Fichter MM, Kaplan A, Berrettini WH, Strober M, Treasure J, Lilienfeld LR, Klump K, Kaye WH. Personality, perfectionism, and attitudes toward eating in parents of children with eating disorders. *International Journal of Eating Disorders*. 2002; 31:290–299. [PubMed: 11920990]

Table 1

Proband demographic information for AN probands (n=433)

Age of onset, mean (S.D.)	16.0 (3.0)
Age of first ED symptom, mean (S.D.)	14.7 (3.2)
Clinical status (past month), n (%)	
Asymptomatic	221 (51.3)
Symptomatic	207 (48.7)
Subtype	
Restricting (RAN)	261 (63.2)
Purging only (PAN)	71 (17.2)
Bingeing/Purging (BAN)	81 (19.6)
BMI (kg/m ²), mean (S.D.)	
Lifetime high	21.1 (2.3)
Lifetime low	13.6 (1.9)
Current	18.1 (2.9)

AN, Anorexia nervosa; S.D., standard deviation; ED, eating disorder; BMI, body mass index.

Table 2

Descriptive information [mean (S.D.)] for study sample

	Proband (n=433)	Father (n=433)	Mother (n=433)
Age	25.5 (6.9)	56.1 (8.7)	53.6 (8.2)
EDI Drive for Thinness	15.4 (5.6)	1.2 (2.7)	2.6 (4.3)
EDI Body Dissatisfaction	17.8 (7.2)	4.4 (5.1)	9.2 (7.6)
EDI Bulimia	2.8 (4.4)	0.7 (2.7)	0.9 (2.2)
MPS Perfectionism Total	101.2 (21.3)	66.7 (17.2)	69.3 (21.8)
STAI State Anxiety	47.4 (14.6)	33.1 (10.0)	34.3 (11.2)
STAI Trait Anxiety	52.7 (13.5)	34.9 (9.6)	37.1 (10.2)
NEO Neuroticism	110.6 (24.9)	77.0 (20.8)	84.0 (22.0)
TCI Novelty-seeking	15.5 (6.9)	16.2 (5.9)	16.8 (5.9)
TCI Harm Avoidance	21.4 (7.6)	12.7 (6.8)	15.4 (6.8)
TCI Reward Dependence	16.8 (3.8)	14.3 (4.2)	17.4 (3.7)
TCI Persistence	6.3 (1.7)	5.1 (2.0)	5.0 (2.1)
TCI Self-directedness	27.6 (8.9)	35.4 (6.7)	34.6 (7.0)
TCI Cooperativeness	35.2 (5.4)	34.4 (5.9)	36.0 (5.1)
TCI Self-transcendence	13.3 (6.3)	12.9 (5.8)	15.5 (6.3)
BIS Cognitive	17.7 (4.3)	14.8 (3.3)	15.0 (3.5)
BIS Motor	19.3 (4.2)	19.8 (3.2)	20.1 (3.5)
BIS Non-planning	22.4 (4.9)	22.8 (4.6)	23.3 (4.3)
YBC-EDS Total	13.4 (8.3)	N.A.	N.A.
YBOCS Total	16.8 (12.4)	N.A.	N.A.

EDI, Eating Disorder Inventory-2; MPS, Multidimensional Perfectionism Scale; STAI, Spielberger State-Trait Anxiety Inventory; NEO, Revised NEO Personality Inventory; TCI, Temperament and Character Inventory; BIS, Barratt Impulsivity Scale-11; YBC-EDS, Yale-Brown-Cornell Eating Disorder Scale; YBOCS, Yale-Brown Obsessive Compulsive Scale; S.D., standard deviation; N.A., not assessed.

Table 3

Trio latent classes

Variable	Class 1 mean (S.D.) (moderate symptom probands/healthy mothers) 33% (n=143)	Class 2 mean (S.D.) (highest symptom probands/ moderate symptom mothers) 43% (n=186)	Class 3 mean (S.D.) (high symptom probands/ high symptom mothers) 24% (n=104)	F (2, 362)	p value
EDI Drive for Thinness					
Proband	12.3 (6.6)	17.3 (3.7)	16.5 (5.3)	34.5	<0.001
Father	1.3 (2.9)	1.0 (2.0)	1.2 (2.2)	0.6	0.5
Mother	2.0 (3.6)	1.6 (3.1)	5.5 (6.1)	27.8	<0.001
EDI Body Dissatisfaction					
Proband	13.7 (7.0)	20.4 (6.2)	18.8 (6.7)	36.9	<0.001
Father	4.5 (5.1)	3.9 (4.4)	4.9 (4.6)	1.5	0.2
Mother	8.1 (6.9)	8.2 (6.9)	13.4 (8.7)	17.0	<0.001
MPS Perfectionism					
Proband	88.4 (21.5)	109.8 (16.1)	103.0 (21.4)	42.1	<0.001
Father	65.9 (16.4)	66.3 (17.4)	67.3 (17.1)	0.2	0.8
Mother	66.1 (19.3)	63.7 (18.1)	86.0 (22.4)	39.4	<0.001
NEO Neuroticism					
Proband	87.1 (15.4)	126.2 (17.5)	112.8 (20.5)	169.5	<0.001
Father	74.6 (21.5)	75.2 (20.7)	80.9 (19.3)	2.7	0.1
Mother	73.3 (15.9)	77.4 (14.7)	112.2 (15.9)	189.8	<0.001
STAI Trait Anxiety					
Proband	40.8 (9.5)	61.0 (9.2)	53.1 (12.1)	137.9	<0.001
Father	34.3 (9.5)	33.8 (9.0)	37.3 (9.8)	4.2	0.0
Mother	32.4 (7.2)	33.7 (6.7)	50.7 (7.9)	200.0	<0.001
TCI Harm Avoidance					
Proband	14.9 (5.7)	25.6 (5.3)	22.4 (7.0)	115.4	<0.001
Father	11.7 (6.6)	12.3 (6.5)	13.6 (7.6)	2.1	0.1
Mother	12.0 (4.7)	13.6 (5.2)	23.5 (4.9)	154.8	<0.001

EDI, Eating Disorder Inventory-2; MPS, Multidimensional Perfectionism Scale; NEO, Revised NEO Personality Inventory; STAI, Spielberger State-Trait Anxiety Inventory; TCI, Temperament and Character Inventory; S.D., standard deviation.

Table 4

Effect sizes and post-hoc tests for AN trio latent classes

Variable		Partial g ²	Magnitude of effect	p value		
				Class 1 v. class 2	Class 2 v. class 3	Class 1 v. class 3
EDI Drive for Thinness						
Proband	0.2	Large		<0.001	0.5	<0.001
Father	0.0	N.A.		N.A.	N.A.	N.A.
Mother	0.1	Medium		0.8	<0.001	<0.001
EDI Body Dissatisfaction						
Proband	0.2	Large		<0.001	0.2	<0.001
Father	0.0	N.A.		N.A.	N.A.	N.A.
Mother	0.1	Medium		1.0	<0.001	<0.001
MPS Perfectionism						
Proband	0.2	Medium		<0.001	>0.001	<0.001
Father	0.0	N.A.		N.A.	N.A.	N.A.
Mother	0.2	Medium		0.6	<0.001	<0.001
NEO Neuroticism						
Proband	0.5	Large		<0.001	<0.001	<0.001
Father	0.0	N.A.		N.A.	N.A.	N.A.
Mother	0.5	Large		0.1	<0.001	<0.001
STAI Trait Anxiety						
Proband	0.4	Large		<0.001	<0.001	<0.001
Father	0.0	N.A.		N.A.	N.A.	N.A.
Mother	0.5	Large		0.3	<0.001	<0.001
TCI Harm Avoidance						
Proband	0.4	Large		<0.001	<0.001	<0.001
Father	0.0	N.A.		N.A.	N.A.	N.A.
Mother	0.5	Large		>0.001	<0.001	<0.001

AN, Anorexia nervosa; EDI, Eating Disorder Inventory-2; MPS, Multidimensional Perfectionism Scale; NEO, Revised NEO Personality Inventory; STAI, Spielberger State-Trait Anxiety Inventory; TCI, Temperament and Character Inventory; N.A., not assessed.

Table 5

External validation ANOVA results for AN trio latent classes

	df	F	p value	Partial η^2
Proband YBC-EDS current total	2, 362	4.6	>0.001	0.0
Proband YBOCS total	2, 330	0.9	0.4	0.0
EDI Bulimia				
Proband	2, 359	0.3	0.7	0.0
Father	2, 361	0.1	0.9	0.0
Mother	2, 361	0.9	0.4	0.0
BIS Motor				
Impulsivity				
Proband	2, 353	0.2	0.9	0.0
Father	2, 354	2.6	0.1	0.0
Mother	2, 359	0.8	0.4	0.0
BIS Cognitive Impulsivity				
Proband	2, 355	0.4	0.7	0.0
Father	2, 360	0.5	0.6	0.0
Mother	2, 361	1.5	0.2	0.0
STAI State Anxiety				
Proband	2, 356	1.8	0.2	0.0
Father	2, 347	1.5	0.2	0.0
Mother	2, 347	1.6	0.2	0.0
TCI Novelty-seeking				
Proband	2, 356	1.2	0.3	0.0
Father	2, 359	0.7	0.5	0.0
Mother	2, 361	1.2	0.3	0.0
TCI Self-directedness				
Proband	2, 357	0.4	0.6	0.0
Father	2, 359	1.6	0.2	0.0
Mother	2, 359	0.4	0.7	0.0
BIS Non-planning Impulsivity				
Proband	2, 354	0.4	0.7	0.0
Father	2, 360	1.8	0.2	0.0
Mother	2, 361	2.2	0.1	0.0

AN, Anorexia nervosa; YBC-EDS, Yale–Brown–Cornell Eating Disorder Scale; YBOCS, Yale–Brown Obsessive Compulsive Scale; BIS, Barratt Impulsivity Scale-11; STAI, Spielberger State-Trait Anxiety Inventory; TCI, Temperament and Character Inventory; df degrees of freedom.