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Factors associated with recovery from anorexia nervosa

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ABSTRACT

Previous studies of prognostic factors of anorexia nervosa (AN) course and recovery have followed clinical populations after treatment discharge. This retrospective study examined the association between prognostic factors—eating disorder features, personality traits, and psychiatric comorbidity—and likelihood of recovery in a large sample of women with AN participating in a multi-site genetic study. The study included 680 women with AN. Recovery was defined as the offset of AN symptoms if the participant experienced at least one year without any eating disorder symptoms of low weight, dieting, binge eating, and inappropriate compensatory behaviors. Participants completed a structured interview about eating disorders features, psychiatric comorbidity, and self-report measures of personality. Survival analysis was applied to model time to recovery from AN. Cox regression models were used to fit associations between predictors and the probability of recovery. In the final model, likelihood of recovery was significantly predicted by the following prognostic factors: vomiting, impulsivity, and trait anxiety. Self-induced vomiting and greater trait anxiety were negative prognostic factors and predicted lower likelihood of recovery. Greater impulsivity was a positive prognostic factor and predicted greater likelihood of recovery. There was a significant interaction between impulsivity and time; the association between impulsivity and likelihood of recovery decreased as duration of AN increased. The anxiolytic function of some AN behaviors may impede recovery for individuals with greater trait anxiety.

1. Introduction

Anorexia nervosa (AN) is a devastating and costly disorder, which places a high emotional and financial burden on patients and their families. One of the foremost challenges for patients and caregivers is managing an illness that can be lengthy, physically destructive, and psychologically exhausting. The disorder ranks among the ten leading causes of disability among young women (Mathers et al., 2000) and has one of the highest mortality rates of any psychiatric disorder (Harris and Barraclough, 1998; Millar et al., 2005; Sullivan, 1995). However, considerable heterogeneity exists in its long-term course and outcome. The most comprehensive reviews of outcome studies in AN to date report that, on average, only

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one-third of individuals (37%) recover within 4 years after disease onset; this figure rises to almost half (47%) by year 10 and to 73% after 10 years post onset (Berkman et al., 2007; Steinhausen, 2002). However, approximately 25% of individuals with AN have a chronic or continuously relapsing course and crude mortality from suicide or medical complications from starvation or compensatory behaviors associated with the illness is 9% (Berkman et al., 2007; Steinhausen, 2002).

Identifying prognostic factors associated with illness duration and recovery could have crucial benefits. First, it would help patients, family members, and treatment providers manage expectations for illness duration and plan treatment options. Second, it would potentially assist providers in identifying which patients are at highest risk for developing a lengthy course or chronic illness. Third, it would aid providers in tailoring treatment to target each patient's individual risk factors for a longer length of illness while also reinforcing the patient's unique protective factors for recovery. Increasing the intensity or specificity of early treatment for the most at-risk patients could, in turn, shorten illness length or prevent chronicity.

The aim of the present study was to examine prognostic factors that are independently associated with AN recovery. The majority of studies examining AN course and prognostic factors has used a prospective longitudinal follow-up design by following patients after treatment discharge from community clinics, specialized clinics, or inpatient care (Berkman et al., 2007). We used a retrospective design with a large sample of women with AN from the multi-site International Price Foundation Genetic Study of AN Trios. Participants were recruited from specialty clinic-based settings and through local and national media advertisements. Given that approximately one-third of the individuals with AN in the community are treated in mental health care settings (Hoek, 2006) and only half of individuals with AN are detected in primary care settings (Hudson et al., 2007), the inclusion of a community-based participants in addition to clinic-ascertained participants potentially increases the ability to observe the course of AN with greater variation in disease severity (Agras et al., 2009).

We examined the following prognostic factors: a) eating disorder features, including age of onset, vomiting, laxative abuse, fasting, and excessive exercise; b) the personality traits of novelty seeking, harm avoidance, reward dependence, persistence, impulsivity, trait anxiety, and perfectionism; and c) psychiatric comorbidity including major depressive disorder (MDD), obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), alcohol abuse or dependence, substance abuse or dependence, and borderline and avoidant personality disorders.

1.1. Hypotheses

Based on the extant literature about AN duration and prognostic factors for recovery, we hypothesized that an earlier age of onset and higher novelty seeking would be positive prognostic factors (i.e., factors that predict a higher likelihood of recovery; Ratnasuriya et al., 1991; Strober et al., 1997; Klump et al., 2004). We also anticipated that the following variables would be negative prognostic factors, predicting a lower likelihood of recovery: a) eating disorder features including vomiting, laxative abuse, and excessive exercise (Deter et al., 2005; Fichter et al., 2006; Strober et al., 1997); b) personality traits including greater harm avoidance, greater perfectionism, greater impulsivity, greater trait anxiety (Klump et al., 2004; Bardone-Cone et al., 2007; Fichter et al., 2006; Strober et al., 1997); and c) psychiatric comorbidity with MDD, anxiety, PTSD, OCD, alcohol and substance abuse or dependence, and personality disorders (Fichter et al., 2006; Halvorsen et al., 2004; Wonderlich et al., 1994; Bulik et al., 2008; Papadopoulos et al., 2009).

2. Method

2.1. Participants

Data were collected as part of the International Price Foundation Genetic Study of AN Trios, designed to identify genetic susceptibility loci of risk for eating disorders. A complete description of recruitment and data collection has been published previously (Reba et al., 2005). In brief, participants were recruited from nine sites in North America and Europe, including Pittsburgh (W.K.), New York (K.H.), Los Angeles (M.S.), Toronto (A.K., B.W.), Munich (M.F.), Pisa (A.R.), Fargo (J.M.), Baltimore (H.B., S.C.), and Tulsa (C.J.), between 2000 and 2003. Potential participants were identified through clinic databases, referral from clinicians with knowledge of the study, and advertisement through a variety of local and national media. The study was approved by local institutional review boards at all sites. Written informed consent was obtained before participation.

Participants were required to meet the following criteria: a) DSM-IV (American Psychiatric Association, 2000) lifetime diagnosis of AN, excluding the amenorrhea criterion; b) low weight less than 5th percentile of body mass index (BMI) for age and gender on the Hebebrand et al. (Hebebrand et al., 1996) chart from the National Health and Nutrition Examination Survey epidemiological sample; c) AN onset before age 25; d) weight controlled through restricting and/or purging, including vomiting, abuse of laxatives, diuretics, enemas, suppositories, or ipecac; e) age between 13 and 65; and f) the diagnosis of AN must have been met at least 3 years before study entry. The last criterion ensured that participants were unlikely to develop binge eating in the future because binge eating typically develops within the first three years after AN onset (Bulik et al., 1997a; Tozzi et al., 2005). Because the primary aim of the study was to investigate genetic loci associated with AN, only Caucasian participants were included (participants could be included with one non-Caucasian grandparent). Further details on inclusion/exclusion criteria have been published previously (Reba et al., 2005).

The study included 736 participants in total. The analysis sample in the present study excludes men ($n = 12$) because there were too few for meaningful comparisons. Participants who were missing age at last symptom or other age information ($n = 8$) were excluded as were women with a history of bulimia nervosa that predated the onset of AN ($n = 33$) because cases of bulimia nervosa to AN crossover were thought to represent a distinct subgroup (Tozzi et al., 2005). The resulting analysis sample included 680 women with AN who met all criteria listed above.

2.2. Measures

2.2.1. Eating disorder diagnoses and features

The Structured Interview for Anorexia Nervosa and Bulimic Disorders (SIAB; Fichter et al., 1998) and an expanded version of Module H of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First et al., 1997b) were administered to assess lifetime diagnosis of eating disorders including AN and age of onset of AN.

Compensatory behaviors such as fasting, vomiting, laxative abuse, and excessive exercise were also assessed with the SIAB. Only the presence of these behaviors was recorded not duration; thus, we were not able to include the duration of these compensatory behaviors as prognostic factors. For fasting, participants were asked, "Have you refrained from eating anything for more than 24 hours in order to avoid weight gain?" Fasting was scored present if participants endorsed fasting rarely (up to one day per month) or more frequently and absent if participants endorsed never fasting. For vomiting, participants were asked, "Have you induced vomiting in order to avoid weight gain?" Vomiting was scored present if participants endorsed any vomiting and absent if

participants endorsed never vomiting. Whether vomiting was compensatory or not was not recorded. For laxative abuse, participants were asked, "Did you use laxatives to avoid gaining weight?" Laxative abuse was scored present if participants endorsed using laxatives at least rarely (less than twice a week) or more frequently and absent if participants endorsed never using laxatives. For excessive exercise, participants were asked, "How much exercise did you engage in? If you couldn't exercise did you feel uneasy or stressed?" Excessive exercise was scored present if participants indicated exercising more than once a day, exercising more than 3 hours per day and reported distress if unable to exercise, declining social opportunities in order to exercise, or exercising when injured. Excessive exercise was scored as absent if none of these conditions was present.

Training and reliability procedures for the SIAB and SCID have been described previously (Kaye et al., 2004). Briefly, interviewers at each site completed a training program and all eating disorder diagnoses were confirmed by the principal investigator at each site after reviewing the SIAB. Second, the project coordinator of the data core reviewed every participant's SIAB interview independently to confirm diagnoses (Kaye et al., 2000).

2.2.2. Recovery, onset, and time to recovery of anorexia nervosa

Because no consensus definition of AN recovery exists (Bardone-Cone et al., 2010; Hoek, 2006; Pike, 1998) recovery was defined as occurring at the offset of AN symptoms only if the participant experienced at least one year without any eating disorder symptom (e.g., low weight, dieting, binge eating, inappropriate compensatory behaviors). Although less conservative than the three-year recovery definition used by Von Holle et al. (Von Holle et al., 2008) with this sample and less lenient than recovery criteria of eight weeks or greater used by others (Strober et al., 1997), we anticipated that a one-year criterion would allow for the capture of true recovery rather than a temporary remission because the highest risk for relapse in clinical samples occurs within the first year after discharge (Carter et al., 2004; Herzog et al., 1999). Subthreshold psychological features (e.g., weight influencing self-evaluation) were allowed because it would be difficult to distinguish these sub-threshold features from non-pathological features of "normative discontent" (Rodin et al., 1985).

Eating disorder duration was equivalent to age of onset subtracted from the age of offset. Age of onset, considered the starting point for person-time, consisted of retrospective report from the SIAB when all criteria for the disorder were first met. Age of offset was the age at last reported symptom of AN in the SCID. The point of offset was determined a recovery event if the retrospective reporting allowed determination of at least 12 months with absence of symptoms of AN, binge eating and inappropriate compensatory behaviors from the SCID. If not, the recovery outcome was classified as undetermined and thus right censored. Person-time for the regression analyses included the duration of the eating disorder up to one year prior to interview.

2.2.3. Personality traits

Participants completed self-report personality and symptom assessments. The Temperament and Character Inventory (TCI-9; Cloninger et al., 1993) is a 240-item self-report measure of the personality traits including novelty seeking, harm avoidance, reward dependence, and persistence. Participants rated whether each item was true or false. The total scores for each of these scales were used in these analyses.

Impulsivity was assessed using the Barratt Impulsivity Scale-11 (BIS-11; Sunday et al., 1995), a 30-item self-report measure of impulsiveness. Participants rated each item on a 4-point scale. The BIS measures cognitive, motor, and non-planning impulsiveness and has been found to assess the degree of impulse control in women with eating disorders (Bulik et al., 1997b). The total BIS score, the sum of the subscales, was used in these analyses.

Anxiety was assessed using the Spielberger State-Trait Anxiety Inventory (STAI Form Y-1; Spielberger et al., 1970), a self-report measure that includes a 20-item scale of current anxiety (state) and a 20-item scale of general levels of anxiety (trait). Participants rated both how they 'feel at this moment' and how they 'generally feel' on a 4-point scale. Because the present study examined only personality traits, only the trait anxiety scale total was included in the present analyses.

Perfectionism was assessed using the Frost Multidimensional Perfectionism Scale (MPS), a 35-item self-report measure of perfectionism. Participants rate whether they agree with each statement on a 5-point scale. Only the concern over mistakes scale was used in the present analyses. The concern over mistakes scale measures the tendency to associate mistakes with a loss of respect and failure (Frost et al., 1990) and has been found to be uniquely elevated in AN compared to other psychiatric disorders (Bulik et al., 2003).

In all of the scales, higher scores reflected greater endorsement of the trait.

2.2.4. Comorbidity

The SCID (First et al., 1997b) was administered to assess lifetime presence of Axis I mood, substance, and anxiety disorders. Diagnoses of MDD, OCD, PTSD, alcohol abuse or dependence, and substance abuse or dependence disorders were used in these analyses. In all cases, Axis I disorders were only coded as present if onset was before the participant experienced her last AN symptom to prohibit estimation of associations between Axis I disorders occurring after recovery and the likelihood of recovery.

The Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II; First et al., 1997a) was administered to assess Axis II cluster B and C disorders. Diagnoses of avoidant personality disorder and borderline personality disorder were used in these analyses.

2.3. Statistical methods

Survival analysis was applied to model time to recovery from AN. Cox regression hazard models (using SAS/STAT® software, version 9.2 of the SAS System for Windows; SAS Institute Inc., 2008) were used to fit associations between predictors and the probability of recovery. The Cox regression model is a semi-parametric regression method estimating the likelihood of recovery and includes information on individuals whose recovery status is unknown (Collett, 1994; Bradburn et al., 2003). In the Cox regression model, the term hazard refers to the likelihood of an outcome, in this case recovery, and a hazard ratio can be considered similar to a relative risk. Duration of the eating disorder as previously defined was used in this model with person-time defined up to one year prior to interview.

We limited the prognostic factors examined in these analyses to groups less than ten covariates per model and to conditions that had been found to be associated with AN recovery in previous studies in an effort to reduce overfitting. Three models were prespecified, with covariates grouped by domain: eating disorder features (Model 1), personality traits (Model 2), and psychiatric comorbidity (Model 3). Covariates with significant effects from any of the first three models were then included in a fourth and final combined model (Model 4). Each model was evaluated for fit through residual analysis and a test for interaction with time for each covariate. All continuous variables from personality traits and 'age at onset' were mean centered. Main effect estimates for

variables with significant time interactions then represented the risk ratio at onset for the mean of that covariate. Any significant time interaction term was retained in the model. To assess multicollinearity, calculation of variance inflation factors (VIF) was done for each of the four models. No VIF exceeded 2.1, a value not deemed a strong indicator of multicollinearity. Thus, all variables were left unaltered (Belsley et al., 1980). All tests were two-sided and statistical significance was set at an alpha level of 0.05. All *p*-values in the final models 1–4 were adjusted by model according to the Benjamini–Hochberg method of false discovery rate (FDR) control (Benjamini and Hochberg, 1995).

3. Results

3.1. Sample characteristics

Of the 680 women with AN, 123 (18.1%) met the study criterion for recovery, defined as 12 months symptom free. Of the participants who were recovered, the mean number of years since the last eating disorder symptom was 5.7 (SD = 5.6). The mean age at interview of this sample was 26.0 (SD = 7.7) years.

3.2. Demographics and eating disorder features

Demographic characteristics and eating disorder features are included in Table 1. In addition, the majority of participants had no children (n = 579; 86.7%) and was employed at the time of the interview (n = 420; 66.6%).

3.3. Personality traits and comorbidity

Mean personality trait scores and prevalence of comorbid Axis I diagnoses are presented in Table 2. The most frequent lifetime comorbid diagnoses included MDD (69.4%), OCD (53.3%), and avoidant personality disorder (24.4%). Models 1–4 are presented in Table 3 and will be described below in further detail.

3.4. Model 1: Eating disorder features

In a Cox regression model, hazard ratios greater than 1 indicate a higher probability of recovery whereas ratios less than 1 indicate a lower probability of recovery. Interaction terms indicate how these hazard ratios changed over time. In Model 1, participants had a lower probability of recovery (hazard ratio = 0.37; 63% lower hazard) if they endorsed vomiting. There were no other significant prognostic factors.

Table 1
Demographics and features of women with anorexia nervosa in the sample (n = 680 women).

	M (SD)	*N* (%)
Education		
Less than high school		65 (9.8)
High school degree		303 (45.7)
Some college		181 (27.3)
Graduate degree		114 (17.2)
Marital status		
Married		119 (17.9)
Widowed, divorced or separated		92 (13.8)
Never married		454 (68.3)
Age		
Age of onset	16.0 (2.8)	
Age at time of interview (years)	26.0 (7.7)	
Duration of anorexia nervosa	8.9 (7.2)	
Compensatory behaviors		
Vomiting		233 (36.6)
Laxative abuse		186 (29.2)
Fasting		284 (41.8)
Excessive exercise		343 (50.4)

Table 2
Personality traits and comorbid diagnoses in the sample of women with anorexia nervosa (n = 680).

Personality traits	***M* (SD)**
Temperament and Character Inventory	
Novelty seeking	15.8 (7.0)
Harm avoidance	21.8 (7.5)
Reward dependence	16.5 (3.9)
Persistence	6.2 (1.8)
Barrett Impulsivity Scale	
Total Score	60.0 (10.9)
State Trait Anxiety Inventory	
Trait anxiety	53.6 (13.5)
Multidimensional Perfectionism Scale	
Concern over mistakes	34.4 (8.8)
Comorbid diagnoses	***N* (%)**
Axis I diagnoses	
Major depressive disorder	460 (69.4)
Obsessive compulsive disorder	358 (53.3)
Post-traumatic stress disorder	103 (15.8)
Alcohol abuse/dependence	86 (12.8)
Substance abuse/dependence	36 (5.4)
Axis II diagnoses	
Avoidant	160 (24.4)
Borderline	59 (9.0)

3.5. Model 2: Personality traits

In Model 2, impulsivity was a significant factor in probability of recovery. At eating disorder onset, participants had a significantly higher probability of recovery when they endorsed more impulsivity (hazard ratio = 1.05; 5% higher hazard). However, the significant interaction between impulsivity and time indicated that the association between impulsivity and recovery decreased significantly over time (time interaction coefficient = −0.036). For example, at years 2, 5, and 10, the hazard ratios declined to 0.99, 0.89, and 0.74. There were no other significant interactions with personality traits and time. In addition, participants had a lower probability of recovery (hazard ratio = 0.94; 6% lower hazard) when they endorsed more trait anxiety.

3.6. Model 3: Comorbidity

In Model 3, participants had a lower probability of recovery when they met criteria avoidant personality disorder (hazard ratio = 0.41; 59% lower hazard).

3.7. Model 4: Combined model

In this model, all significant predictors of time to recovery were included in a fourth combined model. Vomiting remained a significant predictor of recovery. Participants had a lower likelihood of recovery if they endorsed vomiting (hazard ratio = 0.36; 64% lower hazard). Impulsivity and trait anxiety remained significant predictors of recovery. Participants had a significantly higher probability of recovery when they also endorsed more impulsivity at the onset of

Table 3
Results (hazard ratios and 95% confidence intervals) from Cox regression hazards models predicting time to recovery from anorexia nervosa features (Model 1), personality traits (Model 2), comorbidity (Model 3), and a combined model (Model 4). Significant hazard ratio statistics ($p < .05$) are highlighted in bold.

	Model 1	Model 2	Model 3	Model 4
Anorexia nervosa features				
Age at onset	0.99 (0.93–1.06)			
Vomiting	**0.37 (0.22–0.62)**			**0.36 (0.22–0.58)**
Laxative abuse	0.88 (0.53–1.48)			
Fasting	1.08 (0.71–1.62)			
Excessive exercise	0.81 (0.55–1.20)			
Personality traits				
Novelty seeking		1.03 (1.00–1.07)		
Harm avoidance		1.03 (0.99–1.07)		
Reward dependence		1.03 (0.98–1.08)		
Persistence		0.96 (0.86–1.08)		
Impulsivity		**1.05 (1.02–1.08)**		**1.07 (1.04–1.10)**
Impulsivity*time interaction (this number represents a proportion change in the impulsivity effect for a one unit change in time)		**0.97 (0.95–0.98)**		**0.97 (0.95–0.98)**
Trait anxiety		**0.94 (0.92–0.96)**		**0.94 (0.92–0.96)**
Concern over mistakes		1.00 (0.98–1.02)		
Comorbidity				
Axis I diagnoses				
Major depressive disorder			0.65 (0.43–0.97)	
Obsessive compulsive disorder			1.00 (0.68–1.48)	
Post-traumatic stress disorder			0.59 (0.28–1.22)	
Alcohol abuse/dependence			1.19 (0.66–2.16)	
Substance abuse/dependence			0.64 (0.17–2.44)	
Axis II diagnoses				
Avoidant			**0.41 (0.22–0.77)**	0.86 (0.46–1.60)
Borderline			0.77 (0.30–1.99)	

eating disorder (hazard ratio = 1.07; 7% higher hazard) and the association between impulsivity and recovery attenuated significantly over time (time interaction coefficient = −0.035). Participants also had a lower probability of recovery (hazard ratio = 0.94; 6% lower hazard) when they endorsed more trait anxiety on the STAI.

Axis I and Axis II measures were not significant in this combined model.

4. Discussion

The present investigation examined prognostic factors (i.e., eating disorder features, personality traits and comorbid psychiatric disorders) for recovery from AN. Vomiting, trait anxiety, and impulsivity were associated with recovery in this sample. In line with our hypotheses, the lifetime presence of vomiting and a higher level of trait anxiety were negative prognostic factors. However, contrary to our predictions, impulsivity was a positive prognostic factor. Furthermore, impulsivity also had a time-dependent association; at onset, impulsivity was positively associated with recovery, but as duration of AN increased, the positive association between impulsivity and recovery declined.

In addition, consistent with our hypotheses, avoidant personality disorder was a significant negative prognostic factor. However, this factor was not significant in the final model. The likelihood of recovery was better accounted for by vomiting, trait anxiety, and impulsivity. Finally, age of onset, laxative abuse, fasting, excessive exercise, novelty seeking, harm avoidance, reward dependence, persistence, concern over mistakes, and the presence of comorbid OCD, MDD, alcohol and substance abuse or dependence, PTSD, and borderline personality disorder were not significant predictors.

4.1. Recovery from AN

These findings are in accord with a number of studies examining AN outcome (Steinhausen, 2002). However, the overall time to recovery was somewhat longer in this sample (8–9 years) compared with previous research, which reported the median length of illness to be 6.5 (79 months) years for full recovery (Strober et al., 1997). Similarly the percentage of participants in recovery from AN in the current study was unusually low (18.4%) compared with estimates of 20–50% in other studies (Herzog et al., 1999; Strober et al., 1997; Clausen, 2004). This is likely due to three factors: first, the recovery definition was comparatively stringent (one year with no eating disorder symptoms); second, the amount of evaluable time a participant is followed in this study is intrinsically different compared to prospective studies; time since AN onset could be significantly shorter in this sample than prospective studies with follow-up times of, at minimum, 6–12 years, which could have led to lower recovery estimates. Third, participants were recruited for a genetics study in which their parents also participated, which may have led to unique sample characteristics.

4.2. Prognostic factors

These results indicate that vomiting is a particularly negative prognostic factor for recovery from AN and are in line with previous reports (van Son et al., 2010). Why vomiting is a negative prognostic factor is unclear, but may be related to the higher levels of psychological disturbance seen in individuals with AN and purging. In a latent class analysis examining women with eating disorders, women in the class with the highest percentage of AN binge/purge subtype were also more likely to have comorbid Axis 1 and 2

diagnoses compared with women in the class with the highest percentage of AN restricting subtype (Keel et al., 2004). Increased severity from combined psychological disturbance could interfere with treatment and decrease the likelihood of recovery.

In line with previous research, trait anxiety was a negative prognostic factor. Others have reported a linear relationship between responses to the trait anxiety scale from the STAI and remission; an increase of one unit on the trait anxiety scale reduced the chance of remission from AN by a factor of 1.15 (Yackobovitch-Gavan et al., 2009). Women recovered from AN also score higher than co-twin controls and healthy control women on trait anxiety measures (Keski-Rahkonen et al., 2007; Lilenfeld et al., 2000). Because anxiety disorders are common in families of individuals with AN (Keel et al., 2005) and anxiety symptoms often emerge in childhood prior to the onset of AN (Raney et al., 2008), these traits likely represent a pathway to AN in addition to decreasing the likelihood of recovery from the disorder. This finding is also consistent with a pathological fear-conditioning model of AN, which hypothesizes that anxiety could predict AN persistence because fear-based learning leads to a phobia of weight gain that is not within cognitive control (Strober, 2004). In addition, core features of AN—food restriction and exercise—are hypothesized to have an anxiolytic effect (Dellava et al., 2010; Kaye, 2008), which could make it more difficult for those with increased trait anxiety to relinquish the AN behaviors that may buffer their anxiety.

Although these results suggest that impulsivity is a positive prognostic factor, impulsivity has been found to be a negative prognostic factor in at least one other study of AN outcome (Fichter et al., 2006). We hypothesize that these contradictory findings across studies may be due to differences in impulsivity assessment. Fichter et al.'s (2006) measure of impulsivity included ratings of auto-aggressive behavior, shoplifting of nonfood articles, and promiscuity. Impulsivity in the present study was measured with the BIS, which may capture different psychological constructs. Impulsivity as measured by the BIS may be associated with recovery from AN because it tempers the rigidity and intractability often associated with AN and could encourage experimenting with healthier eating behaviors, whereas Fichter et al.'s (2006) measure might more appropriately index sensation-seeking behaviors. However, we were unable to identify any psychometric studies of these two measures together, which could provide evidence for this interpretation.

4.3. Strengths and limitations

Strengths of the present study include a large sample of women with AN, a comprehensive interview-based assessment protocol, and a stringent definition of AN recovery. However, the present definition of recovery did not include assessment of psychosocial functioning because none was available. Although no standardized definition of recovery exists (Berkman et al., 2007), future research should take care to assess rigidity in eating behaviors or lingering psychosocial dysfunction.

The participants were also recruited from varied sources compared with prospective studies of AN after discharge from specialty clinic-based programs. However, because some of the participants in the present study were also recruited from specialty centers yet recruitment source and treatment seeking were not directly measured, we were unable to assess treatment heterogeneity and examine treatment experience as a prognostic factor.

The use of retrospective design also has limitations. First, because these data were collected cross-sectionally, it is difficult to determine the exact temporal relationship between model predictors and the likelihood of recovery. These analyses also assume that participants were able to report temporality of their psychiatric diagnoses accurately. Moreover, although a convincing theoretical argument could be made that temperament and personality are stable, it is possible that women with AN might respond differently to these assessments when experiencing the emotional and cognitive stress of extreme dietary restriction and malnutrition than they would when fully weight-restored during recovery (Klump et al., 2004).

Second, our analyses assume that participants did not have a period of recovery (12 months without symptoms of AN) and relapse back to AN prior to the recovery event captured by our measures. If some participants experienced a prior period of recovery and this period was associated with our examined prognostic factors, these analyses would be biased. In addition, it is important to note clinically, that the experience of stressful life-events or onset of a medical or mental health illness during the year following AN symptom offset could influence whether a participant was able to remain symptom free or return to AN behaviors. However, we are unable to predict the direction of model bias or to examine statistically whether factors during this time were associated with continued symptom remission. We believe the likelihood of an earlier recovery event is low given evidence that the highest risk for relapse from AN occurs within the first year after symptoms remit (Carter et al., 2004; Herzog et al., 1999).

Third, the interquartile range for the interval between the onset of the disorder and the assessment interview ranged from 4 to 14years, which is a significant length of time and could lead to incomplete or biased reporting. Retrospective recall is associated with decreased reliability as a result of memory deterioration, hindsight and recall bias, and a tendency to overemphasize past events, which provide an explanation for current problems (Hardt and Rutter, 2004) or underestimate past morbidity (Simon and Vonkorff, 1995). In the present study, it may have led participants to underestimate the extent to which they had experienced episodes of MDD or OCD, overestimate the emotional impact of past traumatic experiences, or forget past alcohol or substance abuse.

Fourth, the requirement that age of onset had to be younger than 25 years of age may have reduced the variance in variable "age of onset" and thus may have limited our ability to examine whether age of onset is a prognostic factor. Also, the definition of fasting as 24 hours without eating may have led to a more conservative interpretation than a less stringent criterion such as missing two consecutive meals or eight waking hours without eating.

4.4. Summary

These data suggest that clinicians, patients with AN, and their families should be educated that vomiting is a particularly pernicious prognostic factor, which is associated with a decreased probability of recovery from AN. Because vomiting can be hidden, they should also be counseled to detect possible external signs so that it can be targeted at its earliest emergence. Ultimately, future research should examine whether focusing treatment on preventing or reducing vomiting or diminishing the negative effects of trait anxiety could shorten AN illness duration or prevent chronicity.

Conflict of interest

All authors report no actual or potential conflict of interest.

Contributors

Dr. Zerwas, Dr. Lund, Ms. Von Holle, Dr. Thornton, and Dr. Bulik designed the statistical analysis plan. Drs. Berrettini, Brandt, Crawford, Fichter, Halmi, Johnson, Kaplan, La Via, Mitchell, Rotondo, Strober, Woodside, Kaye, and Bulik wrote the data collection protocol

and managed data collection. Drs. Zerwas and Thornton managed literature searches and Ms. Von Holle conducted the statistical analysis. Dr. Zerwas, Dr. Thornton, Ms. Von Holle, and Dr. Bulik wrote the first draft of the manuscript. All authors contributed to subsequent drafts and have approved the final manuscript.

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