



## Temporal sequence of comorbid alcohol use disorder and anorexia nervosa

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### HIGHLIGHTS

- We explored the temporal sequence of comorbid anorexia and alcohol disorders.
- Alcohol use disorder was more common in binge eating/purging type anorexia nervosa.
- No differences emerged between anorexia first and alcohol disorder first groups.
- Differences emerged between the anorexia nervosa only and the comorbid group.

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### ABSTRACT

Women with eating disorders have a significantly higher prevalence of substance use disorders than the general population. The goal of the current study was to assess the temporal pattern of comorbid anorexia nervosa (AN) and alcohol use disorder (AUD) and the impact this ordering has on symptomatology and associated features. Women were placed into one of three groups based on the presence or absence of comorbid AUD and the order of AN and AUD onset in those with both disorders: (1) AN Only, (2) AN First, and (3) AUD First. The groups were compared on psychological symptoms and personality characteristics often associated with AN, AUD, or both using general linear models. Twenty-one percent of women ( $n = 161$ ) with AN reported a history of AUD with 115 reporting AN onset first and 35 reporting AUD onset first. Women with binge-eating and/or purging type AN were significantly more likely to have AUD. In general, differences were found only between women with AN Only and women with AN and AUD regardless of order of emergence. Women with AN and AUD had higher impulsivity scores and higher prevalence of depression and borderline personality disorder than women with AN Only. Women with AN First scored higher on traits commonly associated with AN, whereas women with comorbid AN and AUD displayed elevations in traits

**Abbreviations:** AN, Anorexia Nervosa; BN, Bulimia Nervosa; AUD, Alcohol Use Disorder; GAN, Genetics of Anorexia Nervosa; SIAB, Structured Interview for Anorexia Nervosa and Bulimic Syndromes; RAN, AN restricting type; PAN, AN purging type; AN-B, AN with binge eating with or without purging or lifetime history of both AN and BN; YBC-EDS, The Yale–Brown–Cornell Eating Disorder Scale (YBC-EDS); Y-BOCS, Yale–Brown Obsessive Compulsive Scale; TCI, Temperament and Character Inventory; BIS, Barratt Impulsiveness Scale-11; STAI-Y, State-Trait Anxiety Inventory Form Y (STAI-Y); GEE, generalized estimating equation modeling.

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more commonly associated with AUD. Results do not indicate a distinct pattern of symptomatology in comorbid AN and AUD based on the temporal sequence of the disorders.

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## 1. Introduction

The National Center on Addiction and Substance Abuse reports that up to 50% of individuals with an eating disorder abuse substances compared with 9% of the general population, and up to 35% of individuals with substance abuse have an eating disorder compared with 3% of the general population (CASA, 2003). The association between substance abuse and eating disorders is thought to be strongest with bulimia nervosa (BN) (Gadalla & Piran, 2007; Harrop & Marlatt, 2010; Holderness, Brooks-Gunn, & Warren, 1994). However, substance use disorders, including alcohol use disorders (AUD), also occur in women with anorexia nervosa (AN) (Baker, Mitchell, Neale, & Kendler, 2010; Bulik et al., 2004; Root, Pinheiro, et al., 2010; Root, Pisetsky, et al., 2010). For example, a recent population-based study indicated that approximately 22% of women with AN have a lifetime history of AUD (Baker et al., 2010). Although the association between AUD and AN is strongest with AN binge-purge type, the prevalence of AUD in women with AN restricting-type is greater than that found in the general population (Root, Pinheiro, et al., 2010). However, to date, the temporal sequence of comorbid AN and AUD has not been thoroughly examined.

Longitudinal studies indicate that women who initially present with an eating disorder are at risk for AUD over a prolonged period of time. Over the course of nine years, Franko and colleagues (Franko et al., 2005) found that 10% of women with an eating disorder reported onset of AUD after their initial presentation for eating disorder treatment. Similarly, in a 10-year follow-up of male and female adolescents (90% female) hospitalized for AN, 8% developed a new onset AUD (Strober, Freeman, Bower, & Rigali, 1996). The association and risk for comorbid AN and AUD is particularly important as there is substantial mortality in women with this comorbid presentation (Keel et al., 2003; Suzuki, Takeda, & Yoshino, 2011).

Of those women with comorbid AN and AUD, approximately 50% report AN onset prior to AUD onset whereas approximately 30% report AUD onset prior to AN onset (Baker et al., 2010; Bulik et al., 2004). Yet, few large-scale studies have addressed how chronology of onset influences the nature of symptoms, associated features, and additional comorbidities. One study revealed that AUD onset prior to AN onset is associated with increased reports of parental criticism (Bulik et al., 2004). Women with comorbid AN and AUD also report increased motor impulsivity, perfectionism, and parental criticism and expectations as well as greater frequency of major depressive disorder, obsessive compulsive disorder, post-traumatic stress disorder, social phobia, specific phobias, and borderline personality disorder (Bulik et al., 2004; Wiseman et al., 1999).

Further clarifying whether AN or AUD develops first in their temporal sequence may provide information on differential mechanisms of comorbid association, unique mechanisms of causation, insight into symptom heterogeneity, and inform differential treatment approaches. For example, heterogeneity of causal mechanisms is likely as women with AN first may subsequently turn to alcohol to dampen the physical effects of starvation and restriction (Bulik et al., 2004; Godart, Flament, Lecrubier, & Jeammet, 2000; Harrop & Marlatt, 2010), whereas women who develop AUD first may find the initial weight loss that can occur secondary to decreased food caloric intake and increased alcohol caloric intake rewarding (Liangpunsakul, 2010; Lieber, 1991; Reinus, Heymsfield, Wiskind, Casper, & Galambos, 1989). Finally, the symptom profile of each disorder could differ depending on chronology of onset, which could also inform treatment approaches.

The objectives of the present study are four-fold: (1) to assess the prevalence of comorbid AN and AUD in women by AN subtype; (2) to

examine whether the ages of onset of AN and AUD differ in women with AN Only, AN First, and AUD First; (3) to determine whether AN-related symptom endorsement differs in women with AN Only, AN First, and AUD First; and (4) to investigate differences in personality characteristics and prevalence of other psychiatric disorders based on the presence or absence of AUD as well as order of onset in women with both AN and AUD.

## 2. Method

### 2.1. Participants

Participants were women from NIH funded Genetics of Anorexia Nervosa Collaborative Study (GAN), which has been previously described (Kaye et al., 2008). Institutional Review Boards and Ethics Boards at each participating site approved this study. All participants provided informed consent prior to participation.

Probands met criteria for a lifetime diagnosis of DSM-IV AN, with or without amenorrhea, at least three years prior to study entry, and were either ill or recovered. AN diagnosis was required to occur prior to age 45, and probands had to be at least 16 years-old to be included. Women were required to have a lowest illness-related body mass index (BMI) at or below 18 kg/m<sup>2</sup>. For men, the lowest illness related BMI had to be at or below 19.6 kg/m<sup>2</sup>. These values correspond to the 5th percentile BMI values of the NHANES epidemiological sample of women and men (Hebebrand, Himmelmann, Hesecker, Schafer, & Remschmidt, 1996), respectively, for the average age range (27–29 years) of the probands in our previous studies (Kaye et al., 1999; Reba et al., 2005). Probands were required to have at least one first, second, or third degree relative with AN (excluding parents and monozygotic twins) who was willing to participate in the study. Potential probands were excluded from the study if they had a history of binge eating episodes at least twice a week for at least three months; a maximum lifetime BMI exceeding 30 kg/m<sup>2</sup>; a history of severe central nervous system trauma; a psychotic disorder or developmental disability; or any disorder that could confound the diagnosis of AN or interfere with the ability to respond to assessments.

The inclusion criteria for affected family members were the same except that relatives were permitted to engage in regular binge eating and they did not have to meet AN criteria three years prior to study enrollment but were required to have had a minimum duration of at least three months at low weight. An additional lifetime diagnosis of BN was allowed. Families with an affected proband and family member who met inclusion criteria were permitted to include additional relatives with a diagnosis of AN, BN, or eating disorder not otherwise specified (ENDOS). All probands and affected family members completed the same assessment measures.

### 2.2. Measures

#### 2.2.1. Eating disorder pathology

Eating disorder diagnoses (i.e., AN, BN, and EDNOS) were assessed using a modified version of Module H of the Structured Clinical Interview for Axis I Disorders (SCID-I) (First, Spitzer, Gibbon, & Williams, 1997) and the Structured Interview for Anorexia Nervosa and Bulimic Syndromes (SIAB) (Fichter, Herpertz, Quadflieg, & Herpertz-Dahlmann, 1998) which are semi-structured clinical interviews. Specifically, the SCID-I was used to assess inclusion and exclusion criteria, AN diagnosis, age of AN onset, and eating disorder duration. If the participant reported a BMI below the cutoff (18 kg/m<sup>2</sup> for

women, 19.5 kg/m<sup>2</sup> for men), amenorrhea (women only), binge eating, or any inappropriate compensatory behaviors in the past year s/he was considered currently ill. The SIAB was used to confirm eating disorder diagnosis and collect data on age at menarche, age at lowest illness-related weight, current BMI, lifetime lowest illness-related BMI, and lifetime highest BMI.

Using data from these assessments, participants were classified as having one of the following AN subtypes: (1) AN restricting type (RAN; AN with no binge eating or purging), (2) AN purging type (PAN; AN with purging but no binge eating), (3) AN binge/purge type (AN-B; AN with binge eating with or without purging or a lifetime history of both AN and BN).

### 2.2.2. Alcohol use disorder and psychiatric disorders

Participants were interviewed with the SCID-I (First, Spitzer, Gibbon, & Williams, 1997) to assess lifetime DSM-IV defined AUD and the following anxiety disorders: generalized anxiety disorder, obsessive compulsive disorder, panic disorder, post-traumatic stress disorder, and social phobia. AUD was considered present if a participant met criteria for abuse or dependence during their lifetime. AUD onset was defined as the age at which the participant met criteria for abuse or dependence. For those persons who met criteria for both, the earlier age was used. Women were placed into one of three onset groups based on the presence or absence of comorbid AUD and the reported order of onset of AN and AUD in those with both disorders: (1) AN Only, (2) AN First, and (3) AUD First.

The Diagnostic Interview for Genetic Studies, version 3.0/B (Nurnberger et al., 1994), was used to assess symptoms of major depression, in accordance with other NIMH-sponsored genetic studies. Algorithms were developed to determine if participants had a diagnosis of lifetime major depression according to DSM-IV criteria. The Structured Clinical Interview for DSM-IV Axis II Disorders (First, Gibbon, Spitzer, Williams, & Benjamin, 1997), a clinician administered semi-structured interview, was used to assess borderline personality disorder and obsessive compulsive personality disorder.

### 2.2.3. Symptom and personality assessments

Additional semi-structured interviews and several self-report questionnaires were used to assess psychiatric symptoms and personality characteristics. The Yale–Brown–Cornell Eating Disorder Scale (YBC-EDS) (Sunday, Halmi, & Einhorn, 1995) assesses core obsessions and compulsions specific to eating and rates the current and lifetime severity of the eating disorder. The lifetime worst total score was used in the present study. Obsessions and compulsions were evaluated using the Yale–Brown Obsessive Compulsive Scale (Y-BOCS) (Goodman et al., 1989). This is a semi-structured interview which assesses the presence and severity of obsessions and compulsions typically found among individuals with obsessive-compulsive disorder. Three subscales, drive for thinness, bulimia, and body dissatisfaction, of the Eating Disorders Inventory-2 (Garner, 1991) were used to assess specific cognitive and behavioral dimensions of eating disorders.

The personality dimensions of novelty seeking, harm avoidance and reward dependence were measured using the Temperament and Character Inventory (TCI) (Cloninger, Przybeck, Svrakic, & Wetzel, 1994). The TCI has been normed on a large national sample and shows high internal consistency, ranging from .76–.89 (Cloninger, Przybeck, & Svrakic, 1991; Cloninger et al., 1994). Aspects of impulsivity were evaluated using the cognitive, non-planning and motor subscales of the Barratt Impulsiveness Scale-11 (BIS) (Patton, Stanford, & Barratt, 1995), and the State-Trait Anxiety Inventory Form Y (STAI-Y) (Spielberger, Gorsuch, & Luchene, 1970) was used to assess trait anxiety.

### 2.3. Statistical analysis

All analyses were performed using SAS version 9.2 (SAS Institute Inc., 2004). General linear models using PROC GENMOD were applied

to the data to: (1) assess whether the prevalence of AUD differed across AN subtypes; (2) determine if ages of onset differ between the AN Only, the AN First, and the AUD First groups; (3) examine whether AN-related symptom endorsement is different in women across onset groups; and (4) assess whether differences exist for personality characteristics and prevalence of other psychiatric disorders across onset groups. Age at interview was included as a covariate in all analyses. AN subtype was entered as a covariate in models assessing differences across the onset groups.

Because data from related individuals were used in this study, generalized estimating equation modeling (GEE) was applied to correct for the nonindependence of the family data. In this procedure, betas and standard errors are adjusted to account for the relatedness of the family members. The specific methods used to implement GEE are detailed in Klump et al. (2000).

## 3. Results

### 3.1. Sample

A total of 873 participants had a lifetime diagnosis of AN. The following non-mutually exclusive groups were removed from analyses: men ( $n=33$ ) as there were too few for meaningful comparisons; those with insufficient information to assess alcohol problems ( $n=78$ ); and absence of age of onset for alcohol abuse or dependence ( $n=2$ ). No significant differences were observed between those women included and excluded from the report for AUD, current AN illness status, or duration of AN illness. However, participants who were excluded were older at the time of assessment and had an older age of AN onset. The final sample comprised 764 women with AN distributed across the following subtypes: 332 with RAN, 220 with PAN, and 212 with AN-B. The mean age for participants included in the report at the time of the assessment was 29.5 years ( $SD=11.0$ ; range 16–76). Ninety-seven percent of the sample were Caucasian, on average, completed 14.4 years of school, and 62.5% were never married and 28.2% were currently married.

Table 1 lists the number of participants with and without AUD by AN subtype. The prevalence of AUD was significantly greater in those with PAN ( $\chi^2=8.41$ ,  $p<.004$ ) and AN-B ( $\chi^2=16.81$ ,  $p<.001$ ) than those with RAN. No significant difference in prevalence of AUD was observed between those with PAN and those with AN-B ( $\chi^2=1.92$ ,  $p<.17$ ).

A total of 603 (78.9%) women reported no history of AUD (AN Only). In the 161 participants with a history of AUD, 115 (71.4%) reported AN onset prior to the onset of AUD (AN First), 35 (21.7%) reported AUD onset prior to AN (AUD First), and 11 (6.8%) reported onset of AN and AUD in the same year. Because so few women had onset of AN and AUD in the same year and the age of onset of AUD ( $M=17.91$  years) in this group was not significantly different from those in the AUD First group ( $M=17.88$  years), these women were placed in the AUD First group.<sup>1</sup> As shown in Table 2, significant differences in mean ages of AN onset were observed among the AN Only, AN First, and AUD First groups (all pairwise comparisons:  $p<.001$ ), with AN Only having the youngest age of onset and the AUD First group having the oldest age of onset. The AN First onset group had a significantly later age of AUD onset than the AUD First group ( $\chi^2=21.42$ ,  $p<.001$ ). For those with AN First, the average time to AUD onset was  $M=6.17$  ( $SD=6.05$ ) years. For those with AUD First, the average time to AN onset was  $M=4.17$  ( $SD=5.03$ ) years.

<sup>1</sup> All statistical analyses were repeated excluding the AN + AUD in the same year individuals from the AUD First group. All reported results and pairwise comparisons remained identical.

**Table 1**

N (%) of participants with and without alcohol use disorder (AUD) by anorexia nervosa (AN) subtype.

AN subtype	No alcohol use disorder	Alcohol use disorder
RAN	286 (86.1)	46 (13.9)
PAN	168 (76.4)	52 (23.6)
AN-B	149 (70.3)	63 (29.7)

Note. RAN = AN with no binge eating or purging. PAN = AN with purging but no binge eating. AN-B = AN with binge eating and/or purging or a lifetime history of both AN and BN.

3.2. Analyses

Table 3 presents the means and standard deviations of the eating disorder related symptoms by group and the results from analysis of variance including pairwise group comparisons. Participants with AN Only or with AN First reported longer duration of eating disorder illness than those with AUD First (Table 3). All groups differed from one another for age at lowest illness related BMI. Those with AN First were youngest at time of low weight and those with AUD First were oldest at time of low weight. However, these differences did not remain when age at onset was entered as a covariate in the models. Total YBC-EDS score was significantly greater in the AN First group compared with those with AN Only. No differences were observed among the onset groups for lowest illness related BMI nor for the Eating Disorder Inventory-2.

For all personality variables except TCI harm avoidance and reward dependence, the AN Only group differed significantly from the AN First group, with the AN First group scoring higher on all scales (Table 4). The AN Only group also scored significantly lower than the AUD First group on the BIS cognitive and motor impulsivity subscales. No significant differences were observed between the AN First group and the AUD First group on any personality measure.

Table 5 presents the results of the logistic regression analyses comparing the prevalence of other psychiatric disorders among the AN Only, AN First, and AUD First groups. Obsessive compulsive disorder and post-traumatic stress disorder were more prevalent in individuals with AN First than those with AN Only. Also, individuals with AN and AUD, regardless of order of onset, were more likely to endorse major depressive disorder and borderline personality disorder than individuals with AN Only. No significant differences were observed between the AN First group and the AUD First group for any psychiatric diagnosis.

4. Discussion

This report addresses an important gap in the literature, namely whether the onset order of AN and AUD is associated with clinically meaningful differences in AN and related psychopathology, personality, and comorbidity dimensions. On average, women reporting AN First were significantly older at AN onset compared with women with AN Only. Women with AN First also reported AUD onset within six years of AN onset whereas women with AUD First reported, on average, AN onset within four years of AUD onset. This is an especially important consideration for practitioners. Our results highlight the importance of clinicians monitoring the increased risk over time for AUD in patients with AN as well as being mindful of the possible emergence of AN in female patients with AUD.

A clear and distinctive pattern of symptomatology based on the temporal sequence of AN and AUD was not observed. In general, differences were found between women with AN Only and women with AN and AUD irrespective of order of emergence. However, women with AN First did exhibit higher scores on obsession, compulsion, novelty seeking, and anxiety measures and had a higher prevalence of obsessive-compulsive disorder than women with AN Only. It is conceivable that

**Table 2**

Mean (SD) and range for age of onset of anorexia nervosa (AN) and alcohol use disorder (AUD) by onset group.

Age of onset	AN Only Mean (SD) Range	AN First Mean (SD) Range	AUD First <sup>a</sup> Mean (SD) Range
AN age of onset	16.86 (3.97) 2–39	15.82 (2.83) 11–28	22.06 (6.50) 14–45
AUD age of onset	–	21.99 (6.32) 14–54	17.88 (5.24) 13–43

<sup>a</sup> Includes those with onsets of AN and AUD at the same age.

women with AN who have elevated anxiety and obsessions/compulsions may turn to alcohol in order to dampen these thoughts and feelings. In contrast, women with AN and AUD displayed greater impulsivity scores and higher prevalence of depression and borderline personality disorder than women with AN Only. Taken together, these results suggest that, irrespective of order of onset, associated symptoms and features are quite similar in women with comorbid AN and AUD.

The patterns of onset for AN and AUD exhibit similarities as well as differences from previous observations in AN and major depression and AN and childhood overanxious disorder. Analogous to AN and AUD, major depression and childhood overanxious disorder are significantly more common in women with binge-eating and/or purging type eating disorders (Fernandez-Aranda et al., 2007; Raney et al., 2008). In contrast, however, highly distinctive patterns of symptomatology were observed for AN and childhood overanxious disorder. Women with AN who have a history of childhood overanxious disorder exhibited more severe eating disorder symptoms (e.g., varied types of compensatory behaviors, longer duration of illness, and higher body dissatisfaction and food preoccupation scores), higher scores on personality measures such as harm avoidance, persistence, anxiety, self-directedness, neuroticism, and novelty seeking, and were more likely to have an additional anxiety disorder diagnosis than women without a history of childhood overanxious disorder (Raney et al., 2008). It is unclear why a more distinctive pattern of symptomatology was observed for childhood overanxious disorder than for AN and AUD. However, differing comorbidities may reflect heterogeneity of causal mechanisms in AN that are associated with

**Table 3**

Mean (SD) of various eating disorder related symptoms by onset group and results of analysis of variance with generalized estimating equation corrections comparing onset groups. Age at interview and anorexia nervosa (AN) subtype were entered as covariates in all models.

Eating disorder related symptom	AN Only	AN First	AUD First	Onset group differences $\chi^2$ (p-value)	Pairwise differences
Duration of AN illness	9.12 (8.20)	11.41 (9.16)	8.87 (6.87)	<b>7.30 (.026)</b>	AUD First<AN Only, AN First
Lowest illness-related BMI	14.54 (1.93)	14.71 (1.86)	15.21 (1.84)	4.67 (.10)	–
Age at lowest illness-related BMI	19.07 (5.67)	18.15 (5.19)	22.54 (6.35)	<b>16.36 (.001)</b>	AN First<AN Only<AUD First
EDI drive for thinness	13.79 (6.31)	15.42 (5.63)	14.98 (6.62)	4.84 (.09)	–
EDI body dissatisfaction	16.11 (7.95)	17.78 (7.62)	17.56 (8.40)	1.78 (.41)	–
EDI bulimia	2.29 (3.90)	4.03 (5.22)	3.51 (3.93)	4.41 (.11)	–
YBC-EDS total worst score	23.53 (6.20)	25.65 (4.24)	25.37 (5.57)	<b>13.77 (.001)</b>	AN Only<AN First

Note. AUD = alcohol use disorder. EDI = Eating Disorder Inventory. YBC-EDS = Yale-Brown-Cornell Eating Disorder Scale. Significant results bolded.

**Table 4**  
Mean (SD) of various personality characteristics by onset group and results of analysis of variance with generalized estimating equation corrections comparing onset groups. Age at interview and anorexia nervosa (AN) subtype were entered as covariates in all models.

Eating disorder related symptom	AN Only	AN First	AUD First	Onset Group Differences $\chi^2$ (p-value)	Pairwise Differences
YBOCS obsessions	5.84 (6.00)	7.70 (6.20)	6.33 (6.30)	<b>7.27 (.027)</b>	AN Only<AN First
YBOCS compulsions	6.42 (6.35)	8.39 (6.25)	6.57 (6.24)	<b>7.93 (.019)</b>	AN Only<AN First
TCI novelty seeking	16.43 (6.62)	20.11 (6.66)	19.02 (6.95)	<b>21.11 (.001)</b>	AN Only<AN First
TCI harm avoidance	20.14 (7.55)	21.63 (7.76)	21.24 (7.09)	3.32 (.20)	–
TCI reward dependence	16.24 (3.55)	15.34 (4.03)	16.44 (3.55)	5.28 (.08)	–
BIS cognitive	16.72 (4.36)	18.66 (4.49)	18.27 (4.38)	<b>16.37 (.001)</b>	AN Only<AN First, AUD First
BIS non-planning	22.60 (4.77)	25.50 (4.99)	24.25 (5.31)	<b>24.08 (.001)</b>	AN Only<AN First
BIS motor	19.68 (3.86)	22.53 (4.57)	21.47 (4.18)	<b>26.42 (.001)</b>	AN Only<AN First, AUD First
STAI-Y trait anxiety	48.92 (13.59)	52.33 (13.62)	52.44 (12.46)	<b>6.80 (.034)</b>	AN Only<AN First

Note. AUD = alcohol use disorder. YBOCS = Yale-Brown-Obsessive Compulsive Scale. TCI = Temperament and Character Inventory. BIS = Barratt Impulsiveness Scale. STAI-Y = State Trait Anxiety Inventory. Significant results bolded.

differing clusters of liability (e.g., propensity to anxiety, alterations in reward biology).

Finally, corroborating previous research, we also show that AUD is not a rare occurrence in women with AN (Baker et al., 2010; Root, Pinheiro, et al., 2010). Approximately 21% of our nonclinical sample reported a lifetime history of an AUD. Additionally, women with PAN and AN-B were significantly more likely to report a lifetime AUD history than women with RAN. No significant differences emerged in the prevalence of lifetime AUD in women with PAN and AN-B. This suggests that women with a binge-eating and/or purging type eating disorder are at similar risk for comorbid AUD. One possibility for the increased risk of AUD in binge-eating and purging type eating disorders is that binge eating, purging, and alcohol use behaviors share vulnerability factors. For example, disturbances in dopamine functioning appear to occur in both eating disorders, especially those of binge-eating/purge type, and AUD (Feltenstein & See, 2008; Kaye, 2008). This dopamine disturbance is thought to impair reward modulation as well as play a role in other symptoms associated with both disorders, such as anxiety (Bohon & Stice, 2011; Bowirrat & Oscar-Berman, 2005; Stein, Westenberg, & Liebowitz, 2002). Similarly, significant associations between elevated personality traits such as novelty seeking and impulsivity with binge-eating and substance use have been reported (Cassin & von Ranson, 2005; Cloninger, Sigvardsson, & Bohman, 1988; Dawe & Loxton, 2004) and, as in our study, these traits are more prominent in women with comorbid eating and substance use disorder than in women with an eating disorder only (Bulik, Sullivan, Weltzin, McKee,

& Kaye, 1994). These shared underlying vulnerabilities may, in part, explain the risk for the comorbid disorder. However, the relationships between dopamine disturbance, reward modulation, novelty seeking, and these disorders remain unknown.

#### 4.1. Limitations

Limitations of this study must be noted. First, the sample is cross-sectional in nature; therefore, conclusions about causation cannot be made. Second, we had to rely on participant self-report to ascertain age of onset for AN and AUD and most of the variables included in this study. Thus, recall bias may be present. Our self-report personality and symptom measures may not capture the distinct factors associated with the emergence of each of these presentations. Third, all women have a lifetime history of AN so we were unable to include a healthy comparison group or an AUD Only comparison group. Additionally, binge-eating which occurs while underweight may have a differing liability process compared to binge-eating that occurs at normal weight. Fourth, the sample includes families that have an enriched history for eating disorders, which may impact the generalizability of the results. Similarly, we did not examine family data to determine whether familial AUD load is greater in AUD First cases. Finally, the small sample size of the groups did not allow for a complete explication of all possible patterns of onset (i.e., AN and AUD onset during the same year).

**Table 5**  
Number (%) of participants with various psychiatric disorders by onset group and results from logistic regressions with generalized estimating equation corrections comparing onset groups. Age at interview and anorexia nervosa (AN) subtype were entered as covariates in all models.

Eating disorder related symptom	AN Only		AN First		AUD First		Onset group differences $\chi^2$ (p-value)	Pairwise differences
	No diagnosis	Diagnosis	No diagnosis	Diagnosis	No diagnosis	Diagnosis		
Generalized anxiety disorder	548 (91.9)	48 (8.1)	99 (86.8)	15 (13.2)	37 (82.2)	8 (17.8)	3.76 (.16)	–
Obsessive compulsive disorder	350 (58.3)	250 (41.7)	46 (40.7)	67 (59.3)	25 (54.4)	21 (45.6)	<b>9.41 (.010)</b>	AN Only<AN First
Panic disorder	531 (90.0)	59 (10.0)	97 (85.1)	17 (14.9)	33 (71.7)	13 (28.3)	4.48 (.11)	–
Post-traumatic stress disorder	523 (89.0)	65 (11.0)	85 (74.6)	29 (25.4)	34 (79.1)	9 (20.9)	<b>9.25 (.010)</b>	AN Only<AN First
Social phobia	483 (81.2)	112 (18.8)	85 (73.9)	30 (26.1)	33 (71.7)	13 (28.3)	2.20 (.34)	–
Depression	206 (34.4)	393 (65.6)	21 (18.3)	94 (81.7)	7 (15.2)	39 (84.8)	<b>13.52 (.002)</b>	AN Only<AN First, AUD First
Borderline personality disorder	562 (97.7)	13 (2.3)	92 (83.6)	18 (16.4)	37 (82.2)	8 (17.8)	<b>19.47 (.001)</b>	AN Only<AN First, AUD First
Obsessive compulsive personality disorder	468 (81.4)	107 (18.6)	87 (79.1)	23 (20.9)	35 (77.8)	10 (22.2)	0.24 (.89)	–

Note. AUD = alcohol use disorder. Significant results bolded.

## 4.2. Conclusion

The temporal sequence of comorbid AN and AUD is not associated with a highly distinctive pattern of symptomatology. However, women who suffer from AN First score higher on traits commonly associated with AN (e.g., anxiety-related traits) compared with women with AN Only, whereas women with AN and AUD, regardless of order of onset (AN First and AUD First), display elevations in traits more commonly associated with AUD (e.g., impulsivity) than women with AN with no history of AUD. Future research should examine the temporal sequence of AN and AUD utilizing longitudinal, prospective reports which include symptoms of AUD and eating disorders in order to fully elucidate the manner in which the emergence of symptoms for one disorder influence the emergence of symptoms of the other. It will be important to include additional vulnerability measures to further delineate the underlying mechanisms of comorbidity.

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### Contributors

Jessica Baker designed the analysis and led the writing of the article. Laura Thornton conducted the analysis and collaborated on the final presentation of the article. Cynthia Bulik was the principal investigator for this analysis, assisted with the design of the analysis, and writing of the article. Walter Kaye was the principal investigator of the study. All additional authors were instrumental in ascertaining participants and collecting data for the GAN study and all approved the final manuscript.

### Conflict of interest

None.

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