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Anorexia Nervosa and Generalized Anxiety Disorder: Further Explorations of the Relation Between Anxiety and Body Mass Index

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Abstract

We explore comorbidity of anorexia nervosa (AN) and generalized anxiety disorder (GAD) and their relation with body mass index (BMI) and evaluate the presence of fasting and excessive exercise which both have anxiolytic and weight loss effects. All participants were female: 32 with AN only, 607 with GAD only, 22 with AN and GAD (AN+GAD), and 5,424 with no history of AN or GAD (referent) from the Swedish Twin study of Adults: Genes and Environment (STAGE). Lowest adult BMI differed significantly ($p < .001$) and was lower in those with AN +GAD than those with AN only ($p < .029$). Those with AN+GAD were most likely to endorse fasting and excessive exercise, followed by women with AN only, women with GAD only, and the referent. Comorbid AN and GAD may be a particularly pernicious presentation influencing both BMI and proclivity to engage in behaviors such as fasting and exercise that serve both weight loss and anxiolytic goals.

Keywords

Anorexia nervosa; Generalized anxiety disorder; Body mass index; fasting; comorbidity

1. Introduction

Anorexia nervosa (AN) and anxiety disorders are commonly comorbid, with upper estimates suggesting that 83% of individuals with AN have a lifetime history of one or more anxiety disorders (Godart, Flament, Lecrubier, & Jeammet, 2000). Godart et al. (2003) observed that over 40% of individuals with AN also reported GAD; individuals with restricting type AN and binge/purge type AN had a significantly higher prevalence of current generalized

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anxiety disorder (GAD) than women without an eating disorder (Godart et al., 2003). In a population based twin study, individuals meeting all Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) (American Psychiatric Association, 1987) criteria for AN were over six times more likely to have GAD (Walters & Kendler, 1995) than women without AN. Food restriction and exercise—both core features of AN—have been hypothesized to play an anxiolytic role in individuals with AN (Dellava et al., 2010; Kaye et al., 2003; Kaye, 2008; Penas-Lledo, Vaz Leal, & Waller, 2002; Shroff et al., 2006). Low body mass index (BMI) is a core feature of AN and is explored as a potential endophenotype of AN (Bulik et al., 2007). For example, low BMI within the context of AN is associated with higher childhood anxiety (Dellava et al., 2010).

Biological studies support our contention that AN, anxiety, and low BMI may be related. In a study of 87 women with AN, the resting energy expenditure (REE) to fat free mass ratio during re-feeding was positively associated with the presence of self-reported anxiety, and anxiety was positively associated with physical activity level (Van Wymelbeke, Brondel, Marcel Brun, & Rigaud, 2004). It is possible that REE is even higher in individuals with comorbid AN and anxiety disorders compared with individuals with AN only. Higher REE independently or via the association with increased physical activity could result in lower BMI.

Although little research has been conducted on the association between GAD and BMI, some studies suggest that individuals with GAD might have lower BMIs than individuals without GAD. In one prospective study, GAD was inversely correlated with overweight (Hasler et al., 2004). In another study, constitutionally thin men were over two times more likely to have GAD compared with non-thin men (Mazzeo, Slof, Tozzi, Kendler, & Bulik, 2004). It is plausible that comorbid AN and GAD may have a synergistic effect and suppress BMI below levels seen in those with AN without comorbid GAD.

Fasting, a core feature of AN which could contribute to attainment and maintenance of low BMI, has been posited to have anxiolytic effects in individuals with AN. During early phases of AN or the illness prodrome, individuals might find that fasting reduces baseline anxiety rendering it both positively (i.e., achieving goal of weight loss) and negatively (i.e., anxiolysis) reinforcing. The reinforcing effects may serve to maintain the illness. Previous hypotheses suggest that elevated serotonin levels result in increased anxiety, which may be reduced by caloric restriction (Kaye et al., 2003; Kaye, 2008). Tryptophan, an essential amino acid, is a precursor to serotonin. Given that tryptophan must be obtained from dietary intake and cannot be synthesized biologically from other sources, restricting dietary intake could decrease tryptophan availability and reduce anxiety. This hypothesis is supported by at least one study which showed that lower intake of dietary tryptophan was associated with reduced anxiety in 14 women with AN and 14 women recovered from AN (Kaye et al., 2003). In a separate study, caloric restriction mediated the relation between childhood anxiety and low BMI during AN (Dellava et al., 2010). Therefore, it is plausible that women with comorbid AN and anxiety disorders engage in even greater caloric restriction (fasting) than individuals with AN without anxiety disorders. More fasting would result in greater caloric deficits and could lead to attainment or maintenance of lower BMIs.

A second feature of AN, excessive exercise, has also been shown to have anxiolytic effects (Norris, Carroll, & Cochrane, 1992; Sexton, Maere, & Dahl, 1989) and is a main contributing factor in the attainment of and maintenance of low BMI. In a sample without eating disorders, both low and high intensity exercise reduced anxiety in individuals who scored high on anxiety sensitivity measures (Broman-Fulks, Berman, Rabian, & Webster, 2004). Among women with eating disorders, women who engaged in excessive exercise reported higher anxiety and obsessionality than women with eating disorders who did not

exercise excessively (Shroff et al., 2006). Therefore, it is plausible that women with comorbid AN and anxiety disorders would engage in excessive exercise to reduce both anxiety and weight. Overall this is likely to result in lower BMIs than women with just AN.

Low BMIs within the context of AN might represent an important endophenotype of AN (Bulik et al., 2007). Further description of individuals who obtain extremely low BMIs within the context of AN might allow for better characterization of this group and improved phenotypic refinement. The aims of the current study are 1) to document comorbidity patterns of AN and GAD in a large population-based sample of Swedish twins; 2) to explore the relation among AN, GAD, and BMI; and 3) to assess whether fasting and excessive exercise are more commonly endorsed by individuals with AN and GAD than those with AN or GAD only or the referent group of individuals with neither AN nor GAD.

2. Method

2.1. Participants

Participants for this study were from the Swedish Twin Registry (STR; <http://ki.se/twinreg>) subsample, the Swedish Twin study of Adults: Genes and Environment (STAGE; <http://ki.se/ki/jsp/polopoly.jsp?d=9610&l=en>). In 2005, twins aged 20–47 were asked about demographic characteristics, health, and life-style habits using web-based surveys with a telephone survey option. The response rate was 59.6%; a detailed description of the study design can be found elsewhere (Furberg et al., 2008; Lichtenstein et al., 2006). STAGE was approved by the Regional Ethics Committee at the Karolinska Institutet and by the Biomedical Institutional Review Board at the University of North Carolina at Chapel Hill. All participants provided informed consent through the web-based interview or the telephone interview.

2.2. Analysis Sample

The sample was based on 13,295 female twins who entered the eating disorder section of the STAGE questionnaire. The following non-mutually exclusive groups were removed prior to analysis: 46 women missing AN diagnosis, 2,977 women missing GAD diagnosis, and 4,187 women who did not have a positive GAD diagnosis but were missing information or indicated a lifetime history of panic disorder, obsessive compulsive disorder, or phobias. Thus, data for 6,085 women were available for analysis. All men were removed from analyses because no men met the diagnostic criteria for AN used in this study.

2.3. Anorexia Nervosa Diagnosis

Lifetime diagnosis of AN was assessed using an expanded on-line Structured Clinical Interview for DSM–IV based instrument (American Psychiatric Association, 1994). AN was considered present if the respondent had a period of time when she weighed much less than people thought she should and had a BMI < 17.55; was very afraid or extremely afraid that she might gain weight or become fat; and during time of low weight felt very or extremely fat. Criterion D, amenorrhea, was not required.

2.4. Generalized Anxiety Disorder Diagnosis

To establish a lifetime diagnosis of GAD, the respondent had to have met both DSM-IV criterion A (excessive anxiety or worry on most days for at least six months) and criterion C [anxiety or worry produced at least three symptoms (restlessness, irritability, fatigue, disturbed sleep, muscle tension, and difficulty concentrating) for at least six months] (American Psychiatric Association, 1994).

2.5. Body Mass Index

Each participant reported lowest weight in kilograms (kg) since age 18 and current height in meters (m). This information was used to compute lowest adult BMI (kg/m^2) for women who did not have a history of AN. Lowest adult BMI for women with a history of AN was calculated from height at the time of low weight and lowest weight during AN. Highest non-pregnancy weight since age 18 and current height were used to compute highest BMI (kg/m^2) for all participants.

2.6. Fasting and Excessive Exercise

Fasting was assessed using responses to questions regarding whether the respondent ever used fasting to control her shape or weight or had not eaten for 24 hours or more. If the participant answered 'never,' fasting was considered absent; otherwise fasting was considered present.

Excessive exercise was similarly assessed. The participant was asked if she exercised more than 2 hours per day to control her shape and weight. If the she endorsed 'daily,' excessive exercise was considered present; otherwise excessive exercise was considered absent.

2.7. Statistical Analyses

All analyses were performed using SAS/STAT® 9.2 software (SAS Institute Inc., 2004). Logistic regression analyses were used to compute odds ratios and 95% confidence intervals (CI) of a participant having AN if lifetime diagnosis of GAD was present and having GAD if lifetime history of AN was present.

For subsequent analyses, individuals were placed into mutually exclusive groups as follows: AN and no GAD (AN only); GAD and no AN (GAD only); AN and GAD (AN+GAD); and no AN and no GAD (referent). Means and standard deviations (SD) were calculated for the BMI measures and number (%) of individuals endorsing fasting and excessive exercise was calculated. All data are presented by group.

Analysis of variance (ANOVA) was used to evaluate group differences in lowest and highest BMI for women with AN only, GAD only, AN+GAD, and the referent group. Age at highest BMI was entered into the model assessing group differences for lifetime highest adult BMI. Logistic regression analyses were used to determine differences in fasting and excessive exercise among groups.

All continuous variables were standardized prior to analyses. Generalized estimating equations corrections were used in all analyses to account for the non-independence of the data due to the inclusion of twins in the analyses. All significance tests were two-tailed.

3. Results

Of the women included in this study, 5,424 comprised the referent group with no history of AN nor GAD [mean (SD) age = 33.9 (7.5)]. Thirty-two women were classified as AN only [mean (SD) age = 34.8 (6.0)], 607 were classified as GAD only [mean (SD) age = 33.3 (7.7)], and 22 women who reported both disorders were classified as AN+GAD [mean (SD) age = 30.1 (6.5)]. Having GAD significantly increased the likelihood of having AN ($\chi^2 = 15.31, p < .001, \text{OR} = 6.12, 95\% \text{ CI} = (3.55, 10.54)$) and having AN significantly increased the likelihood of having GAD ($\chi^2 = 15.40, p < .001, \text{OR} = 6.12, 95\% \text{ CI} = (3.55, 10.55)$).

Means (SD) of lowest and highest adult BMIs for each group are presented in Table 1 along with ANOVA results. Group differences emerged for both lowest and highest adult BMI. Post hoc pairwise comparisons indicated women with AN+GAD had significantly lower

lowest adult BMIs compared with women in the referent group ($p < .001$), women with GAD only ($p < .001$), and women with AN only ($p < .029$). Similarly, women with AN only had significantly lower lowest adult BMIs than women with GAD only ($p < .001$) and the referent group ($p < .001$). Women in the GAD only group had more extreme values than the referent group on lowest adult BMI (GAD only group lower) ($p < .001$) and highest adult BMI (GAD group higher) ($p < .001$). No other significant pairwise differences were observed for highest adult BMI.

Table 1 also presents the number (%) of individuals who endorsed fasting and excessive exercise by group. Group differences were found for fasting with post hoc pairwise comparisons indicating that more women with AN only and women with AN+GAD endorsed fasting than the referent group and GAD only group (all p -values $< .005$). In addition, women with GAD only were more likely to fast than women in the referent group ($p < .001$). Group differences were also observed for excessive exercise. More women in the AN only and AN+GAD groups reported excessive exercise than women in the referent group and women with GAD only (all p -values $< .004$). Women with GAD were more likely to engage in excessive exercise than women in the referent group ($p < .001$).

4. Discussion

The results of this investigation shed further light on the comorbidity of AN and GAD and extend our understanding of the anxiolytic role that fasting and exercise may play in women with AN and GAD and with GAD only. First, AN and GAD are commonly comorbid with the presence of one substantially and significantly increasing the likelihood of the other. Second, there appears to be a gradient of severity with reference to lowest adult BMI with those individuals with comorbid AN and GAD attaining significantly lower BMIs than individuals with AN only. Of interest, individuals with GAD only reported lowest adult BMIs that were lower than the referent group and highest adult BMIs that were higher than the referent group suggesting greater BMI fluctuation than controls.

Particularly noteworthy was the pattern of fasting and excessive exercise across the groups. For both behaviors, a gradient emerged with the greatest percentage of individuals in the AN+GAD group endorsing the behavior, followed by those with AN only, GAD only, and the referent group. Although the post-hoc differences between the AN+GAD and the AN only group were not significant, this was most likely due to low statistical power. Although fasting and excessive exercise were expected to be higher in both groups with individuals with AN, it was less expected that individuals with GAD only would report more fasting and excessive exercise than the referent group. One interpretation is that individuals with GAD also experience the anxiolytic effects of exercise and fasting and are therefore more likely to engage in those behaviors.

Our results have both theoretical and clinical implications. Theoretically, our data further contribute to etiological conceptualizations of AN, which focus on the presence of pre-morbid anxiety and the role that food deprivation plays in anxiety modulation. Anxiety predates onset of AN (Godart et al., 2000; Raney et al., 2008; Salbach-Andrae et al., 2008) and anxiety is associated with the REE to fat free mass ratio during re-feeding (Van Wymelbeke et al., 2004), excessive exercise (Penas-Lledo et al., 2002; Shroff et al., 2006), and high physical activity levels (Brewerton, Stelfox, Hibbs, Hodges, & Cochrane, 1995). We have previously asserted that the combination of starvation and increased physical activity could synergistically reduce anxiety and perpetuate the reinforcing nature of AN (Dellava et al., 2010). The current report is the first to document that these behaviors are also increased in individuals with GAD, potentially suggesting that even those without AN

who suffer from GAD may find the two features of fasting and excessive exercise to be reinforcing perhaps via anxiolytic effects.

Clinically, our results suggest that individuals who present with the constellation of AN and GAD may be particularly vulnerable to development of low BMI during the course of illness possibly via increased fasting and exercise. Although dieting and exercise may provide temporary anxiolysis for individuals with AN with or without comorbid GAD, ultimately, these behaviors contribute to the exacerbation and maintenance of the disorder via an effect on BMI. Therapeutic targeting of anxiety through the development and implementation of alternative anxiety management strategies that do not have the unfortunate side effect of weight loss may be particularly important for patients with this presentation. The increased risk for both GAD and AN underscore the importance of comprehensive assessment of anxiety in individuals with eating disorders and of eating disturbances in individuals with anxiety disorders.

The interpretation of our results should be tempered due to some study limitations. First, our diagnoses of AN and GAD were entirely based on computer-based self-report assessments, and although sensitive information may be more reliably reported via computer (Tourangeau & Smith, 1998), face-to-face interviews do allow for more detailed follow-up and clarification of ambiguous responses. Second, our response rate was 59.6%, and although this is respectable for a population-based study, undetected biases may exist. Third, our sample sizes for the AN only and AN+GAD groups were small. As noted, numeric differences did not always achieve statistical significance suggesting that larger samples could have yielded more definitive results. Fourth, our measures of fasting and excessive exercise were not comprehensive and more detailed measures could provide greater insight into the role of these behaviors in both AN and GAD. Fifth, our results apply only to women and may not generalize to men.

5. Conclusion

The combination of AN and GAD is fairly common and may be a harbinger for increased behaviors that can intensify weight loss associated with AN, such as fasting and exercise, possibly due to anxiolytic effects. These anxiolytic effects may extend to individuals with GAD.

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Table 1

Characteristics of anorexia and anxiety groups relative to the referent.^a

	AN only N=32 (0.5%)		GAD only N=607 (10.0%)		AN+GAD N=22 (0.4%)		Referent ^b N=5424 (89.1%)		Results
	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	
Lowest Adult BMI	15.8 (1.4)	32	19.5 (3.0)	581	14.7 (1.9)	22	20.1 (2.4)	4690	AN+GAD < AN only < GAD only < Referent
Highest Adult BMI	24.3 (4.2)	29	25.7 (5.3)	564	24.1 (5.1)	19	24.8 (4.2)	4699	GAD only > Referent
	No N (%)	Yes N (%)	No N (%)	Yes N (%)	No N (%)	Yes N (%)	No N (%)	Yes N (%)	
Fasting	20 62.5	12 (37.5)	544 (89.6)	63 (10.4)	9 (40.9)	13 (59.1)	5312 (98.6)	76 (1.4)	AN only, AN+GAD > GAD only > Referent
Excessive Exercise	19 (61.3)	12 (38.7)	550 (90.8)	56 (9.2)	9 (40.9)	13 (59.1)	5244 (97.5)	135 (2.5)	AN only, AN+GAD > GAD only > Referent

^a AN, anorexia nervosa; GAD, generalized anxiety disorder; AN+GAD, comorbid AN and GAD; BMI, body mass index

^b Referent group does not have a diagnosis of AN nor GAD