Patterns of Menstrual Disturbance in Eating Disorders

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ABSTRACT

Objective: To describe menstrual disturbance in eating disorders (ED).

Method: We describe menstrual history in 1,705 women and compare eating, weight, and psychopathological traits across menstrual groups.

Results: Menstrual dysfunction occurred across all eating disorder subtypes. Individuals with normal menstrual history and primary amenorrhea reported the highest and lowest lifetime body mass index (BMI), respectively. Normal menstruation and oligomenorrhea groups reported greater binge eating, vomiting, and appetite suppressant use. Amenorrhea was associated with lower caloric intake and higher exercise. Harm avoidance, novelty seeking, perfectionism, and obsessionality discriminated among menstrual status groups. No differences in comorbid Axis I and II disorders were observed.

Conclusion: Menstrual dysfunction is not limited to any eating disorder subtype. BMI, caloric intake, and exercise were strongly associated with menstrual function. Menstrual status is not associated with comorbidity. Menstrual irregularity is an associated feature of all ED rather than being restricted to AN only.

Keywords: eating disorders; menstrual dysfunction; body mass index; purging behaviors; binge eating; personality; comorbidity

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Introduction

We are challenged to improve our understanding of the complex interaction of biological and environmental factors that influence anorexia nervosa (AN), bulimia nervosa (BN), and eating disorders not otherwise specified (EDNOS). These disorders often follow a protracted course and display considerable comorbidity with other psychiatric disorders.[1–5]

Physiological and endocrine abnormalities, including primary or secondary amenorrhea and menstrual dysfunction, are commonly associated with eating pathophysiology and are, for the most part, a function of the severity of weight loss, malnutrition and/or abnormal eating habits.

Amenorrhea occurs in AN and is thought to be a consequence of malnutrition-induced impairments in gonadotropin, particularly luteininzing hormone (LH) secretory patterns.[6] Amenorrhea can occur in normal weight women with low percentage of body fat,[7] can occur prior to significant weight loss, and can persist after weight restoration in women with AN.[8–13] Conversely, menses can resume in some despite low body weight.[14–16]

Although body weight is kept within a normal range in BN, amenorrhea has been reported in 7–40% of patients.[5,17–20] Irregular cycles (oligomenorrhea) are even more frequent, occurring in 37–64% of women with BN.[18,21–24] Studies exploring biochemical measures have shown that menstrual abnormalities in BN are associated with reduced LH concentrations and reduced LH pulse frequency,[25,26] and low levels of estradiol[27] and noradrenalin.[28] The prevalence of polycystic ovaries in women with BN is high (76–100%),[24,29] and in these individuals, oligomenorrhea is thought to be related to an insulin-induced elevation in circulating androgen concentrations,[30] possibly a consequence of large fluctuations in food due to restrictive diets and binge eating behavior.[24] Clinical variables that have been associated with menstrual disturbance in normal weight BN include a high frequency of vomiting, low thyroxine concentrations, and low dietary fat intake,[31] a history of AN, and a past weight loss reaching less than 92% of the ideal body weight.[32]

Several studies have examined other factors associated with the presence or absence of amenorrhea in women with eating disorders (ED). These studies focused on samples comprising individuals with broader definitions of AN and included women meeting all the diagnostic criteria of AN except amenorrhea (partial syndrome AN).[3,14,15,33–36] Women with amenorrhea had a significantly lower body mass index (BMI) than those without amenorrhea.[33,36] In contrast, Garfinkel et al.[3] observed that the degree of weight loss was similar in women with and without amenorrhea. There were no notable differences between those with and without amenorrhea on eating disorder symptomatology, personality, psychiatric comorbidity, or family history. The extent to which the presence of menstrual dysfunction is related to psychological features, personality traits, and other psychiatric comorbidity remains to be clarified.

Since eating disorder symptoms are similar in women with AN with and without amenorrhea, it is important to evaluate the validity of amenorrhea as a diagnostic criterion. Amenorrhea occurs in women with normal-weight BN, in other psychiatric patients, and in female athletes.[35] Obviously, the criterion does not apply to males [although the International Classification of Diseases—Version 10[37] provides an alternative—loss of sexual interest and potency]. Surprisingly, the role of menstrual irregularity as diagnostically relevant for BN or EDNOS has not been debated, despite the prevalence of the symptom.[5,17–19,21,22,24,27,38]

Using population-based data from the Mid-Atlantic Twin Registry, Bulik et al.[14] applying latent class analysis, reported that individuals with the psychological features of AN with and without amenorrhea clustered naturally together. These results concur with prior analyses of the same twin registry[15] identifying a group of females with low weight and the psychological symptoms of ED, only one quarter of whom reported amenorrhea. In addition, we have recently reported that age at menarche shows characteristics of heritable quantitative traits such as normal distribution and familial correlation in individuals with ED and reported a suggestive linkage signal in a BN cohort at 10q13 for this trait.[39] These findings underscore the value of understanding the neurobiology of menstrual function in ED with reference to genetic studies.

The purpose of this study was to describe patterns of menstrual disturbance in a large sample of women with ED. Although the ED diagnosis an individual receives is, in part, related to menstrual status, whether significant within and between diagnostic subtype variation in menstrual function exists is worthy of exploration. Our aims were: (1) to examine the differences in menstrual status across eating disorder subtypes, and (2) to determine the association between clinical and nutritional variables, psychological, and personality features, Axis I and II comorbidity with menstrual dysfunction in women with AN, BN, and EDNOS.

Finally, we wished to discuss the implications of amenorrhea/menstrual dysfunction as a diagnostic criterion for ED.

Method

Participants

Participants were from the three multisite international Price Foundation Genetic Studies of Eating Disorders: AN Affected Relative Pair Study, BN Affected Relative Pair Study, and AN Trios. These studies were designed to identify susceptibility loci involved in risk for ED. Informed consent was obtained from all study participants, and all sites received approval from their local Institutional Review Board. Brief descriptions of each study are provided below.

AN Affected Relative Pair Study. The sample for this study included both probands and affected relatives. Probands met the following criteria: (1) a lifetime diagnosis of AN by DSM IV[1] criteria, waiving the single criterion of amenorrhea for 3 consecutive months; (2) low weight that is/was less than 5th percentile of BMI for age and gender according to the Hebebrand et al.[40] chart of NHANES epidemiological sample; (3) age between 13 and 65 years; (4) onset prior to age 25; and (5) fulfillment of the criteria of AN not less than 3 years prior to ascertainment. Affected relatives were biological family members who: (1) were between the ages of 13 and 65 years and (2) had lifetime eating disorder diagnoses of modified DSM-IV AN (i.e., criterion D not required), lifetime eating disorder diagnoses of DSM-IV BN, purging type or nonpurging type, or EDNOS [eating disorder not otherwise specified—subthreshold AN, subthreshold BN, or subthreshold mixed (relatives who were normal weight but reported either purging behavior or excessive exercise or periods of fasting due to extreme fear of weight gain or undue influence of body weight on self-esteem)]. For the complete list of inclusion and exclusion criteria for probands and relatives, see Kaye et al.[41]

BN Affected Relative Pair Study. The sample for this study included both probands and affected relatives. Probands met the following criteria: (1) DSM-IV[1] diagnosis of BN, purging type, with the additional requirement of at least a 6 month period of binge eating and vomiting at least twice a week and (2) age between 13 and 65 years. Affected relatives were biological family members who: (1) were between the ages of 13 and 65 years and (2) had lifetime eating disorder diagnoses of DSM-IV BN, purging type or nonpurging type, modified DSM-IV AN (i.e., criterion D not required), or EDNOS (subthreshold AN, subthreshold BN, or subthreshold mixed). For the complete list of inclusion and exclusion criteria for probands and relatives, see Kaye et al.[42]

AN Trios Study. The sample for this study included individuals with AN and their parents. Probands were required to meet the following criteria: (1) modified DSM-IV[1] lifetime diagnosis of AN, with or without amenorrhea; (2) low weight that is/was less than 5th percentile of BMIs for age and gender according to the Hebebrand et al.[40] chart of NHANES epidemiological sample; (3) onset prior to age 25; (4) weight that is/was controlled through restricting and/or purging, which includes vomiting, use of laxatives, diuretics, enemas, suppositories, or ipecac, and also, although not considered a purging behavior, excessive exercise; (5) age between 13 and 65 years; and (6) study diagnostic criteria were met at least 3 years prior to entry into the study. Potential participants were excluded if they reported maximum BMI since puberty >27 kg/m^2 for females and >27.8 kg/m^2 for males.

Measures

Clinical Variables. Data relative to minimum and maximum lifetime BMI and number of calories/day when participants were restricting the most were obtained from the Structured Interview for Anorexia Nervosa and Bulimic Syndromes (SIAB), a widely used clinical interview for ED.[43–47] For the number of calories/day, participants were asked both the following questions: Did you try to set a limit on your calorie intake? What was your lowest limit in calories per day at the time when you were restricting the most?

Eating Disorder Diagnoses. Lifetime histories of ED in probands and affected relatives were assessed with the SIAB.[43] For the BN Affected Relative Pairs and AN Trios Studies, additional information regarding eating disorder recovery status as well as the presence or absence of eating disorder symptoms was obtained by an expanded version of module H of the Structured Clinical Interview for DSM-IV Axis I disorders (SCID).[48] This additional information was used as a validation of the ED diagnoses obtained with the SIAB. The diagnostic categories were: (1) DSM-IV AN-restricting (RAN), binge eating, regardless of purging behavior (BAN), and purging type, but no bingeing (PAN) (criteria were modified to include individuals with other menstrual status than only amenorrhea); (2) (DSM-IV BN-purging (PBN) and non purging (NPBN) type; (3) individuals with a history of both AN and BN (ANBN); (4) EDNOS which encompassed subthreshold AN (presence of at least two of the three criterion symptoms of low body weight, extreme fear of fatness, or body image disturbance, undue influence of body weight and shape on self-evaluation, or denial of the seriousness of low body weight), subthreshold BN (the frequency or

duration of eating binges and/or purging or other inappropriate compensatory behaviors fell below the specified DSM-IV criterion, which is twice per week for 3 months, respectively), and subthreshold mix [individuals of normal weight who purged (e.g., vomited or abused laxatives, diuretics, enemas), fasted or exercised excessively due to extreme fear of weight gain, or undue influence of body weight on self-evaluation, in the absence of binges or binge eating].

Binge Eating and Compensatory Behaviors. Binge eating behavior was defined as episodes of eating in which the participant ate a large amount of food (>1,000 kcal, the SIAB's cutoff point for objective binge eating) in a relatively short period of time with loss of control over the eating behavior. If the participant endorsed (1) occasionally (at least an average of twice a week for at least 3 months), frequently (up to once a day for at least 3 months), very frequently (more than once a day for at least 3 months), or at least twice a week but for fewer than 3 months for frequency of binge eating and (2) slight, marked, severe, or very severe for loss of control, she was scored as positive for binge eating behavior.

The definition of laxative abuse and other purging behaviors was as follows: participants were divided into laxative abuse groups based on their response to the question "Did you use laxatives to avoid gaining weight?" Those who endorsed the "never" response option were considered to be nonlaxative abusers; those who used laxatives rarely (less than twice a week and/or in low doses), sometimes (at least twice a week and/or in moderate dose), frequently (up to once daily and/or in high does), or very frequently (several times a day and/or in very high dose) were considered to be laxative abusers. It is important to note that individuals who reported "rare" usage of laxative abuse were also included in the laxative group. Although this response option was below the DSM IV threshold for purging behaviors (on average, twice a week for 3 months), it nonetheless represented individuals who may have used laxatives somewhat infrequently but inappropriately, for the purpose of weight control. The presence of other purging behaviors was also evaluated. The classifications of vomiting behavior and diuretic abuse were similarly defined on the basis of response. Individuals who only reported "experimental" use were not considered to be users, otherwise duration of the behavior was not considered in our operative definition.

Fasting was defined similarly to purging behaviors. Those who endorsed the "never" response option for the question "Have you refrained from eating anything for more than 24 h to avoid weight gain?" were considered as non fasting participants; those who fasted rarely (up to 1 day per month), sometimes (up to 1 day per week), frequently (up to 1 week continuously), or very frequently (longer than 1 week) were included as fasters.

Participants were divided into exercise groups based on their response to the SIAB question "How much exercise did you engage in?" Participants were considered as excessive exercisers if any of the following were reported: (1) severe interference with important activities, (2) exercising more than 3 h per day and distress if unable to exercise, (3) frequent exercise at inappropriate times and places and little or no attempt to suppress the behavior, or (4) exercising despite more serious injury, illness or medical complication. All other participants were categorized as not excessive/regular exercisers.

Menstrual Status. Participants were divided into menstrual status groups according to their response to the SIAB question "Was your period always regular?" Additional questions were asked when necessary: "Have you ever missed your period for at least 3 consecutive months?" If yes: "At that time were you pregnant, lactating or menopausal?" If low weight had been present but participant had not missed three consecutive periods: "What was the pattern of your periods when your weight was very low? Were you taking birth control pills or other hormones?" Menstrual status was then categorized as: (1) normal; (2) oligomenorrhea (period occurred without hormone preparations but was fairly irregular or showed spotting); (3) secondary amenorrhea (period did not occur for at least 3 months after menarche); and (4) primary amenorrhea (period never came or menarche after age 16, and those with menarche after 16 years old but who had ED after age 16 as well). Individuals receiving hormone administration and those on birth control pills were excluded from this analysis since it was not clear whether their period would occur without hormone replacement ($n = 124$), making it difficult to determine their true menstrual status.

Personality and Symptom Assessments. Personality and symptom assessments included the Temperament and Character inventory (TCI),[49] the Frost Multidimensional Perfectionism Scale (MPS),[50] the state-trait anxiety inventory (STAI Form Y-1),[51] the Yale-Brown obsessive compulsive scale (Y-BOCS),[52] and the Yale-Brown-Cornell eating disorder scale (YBC-EDS).[53]

Axis I and II Psychiatric Disorders. Axis I disorders were assessed with the SCID.[54] Personality disorders were assessed with the Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II).[55] Individuals ($N = 380$) from the Price Foundation study "Anorexia Nervosa Affected Relative Pairs"[41] were unable to be included in these analyses as data on Axis I and Axis II comorbidity were not available for that sample.

Statistical Analyses

Menstrual status across diagnostic subtypes was examined using the MULTTEST procedure in SAS.[56] For

the first set of analysis, menstrual status groups were compared on the presence or absence of the various eating disorder behaviors, BMI measures and calorie number, using analysis of variance or logistic regression (depending on the characteristics of the outcome variable). Because these various eating disorder behaviors are used to define the eating disorder subtypes, eating disorder subtype was not entered into any model as a covariate. Thus, the only independent variable fit in these models was menstrual status group.

For the second set of analyses, age of onset as well as the standardized scores of the MPS, TCI, STAI, YBC-EDS, and Y-BOCS were compared across menstrual status groups, using analysis of variance. Logistic regression analyses predicting Axis I and Axis II disorders from menstrual group were performed (for the subsample that included BN Affected Relative Pair and AN trios only). Eating disorder group (AN, BN, ANBN, EDNOS) and age of onset were entered into these regression models as covariates. The interactions (menstrual group $\times$ eating disorder group, menstrual group $\times$ age) were not significant and therefore were removed from all models. Personality variables that emerged in the initial analysis of variance tests as significantly associated with menstrual disturbance were then entered into a stepwise discriminant analysis using the STEPDISC procedure in SAS.[56]

Generalized estimating equations corrections were used in the analyses of variance and the logistic regressions to account for the nonindependence of the data due to the use of affected relatives in the analyses.[57–59] These statistical analyses were conducted using the GENMOD procedure of SAS version 8.1.[56] Chi-square and p values were given for the models. p values were adjusted for multiple testing using the method of false discovery rate.[60]

Results

Participants

The sample initially comprised 1,916 participants. Those excluded from the analyses were: males ($n = 53$); individuals with missing data for the question "Was your period always regular?" ($n = 3$); if the person responded "no period because of pregnancy" or hysterectomy ($n = 8$); if menarche occurred earlier than 16 but eating disorder onset was before menarche, so it is unclear whether menstruation was delayed due to eating disorder ($n = 20$); participants who were younger than 16 at interview and still had not gotten their period ($n = 3$); and, participants who were either receiving hormone administration or birth control pills ($n = 124$). The resulting sample was 1,705.

TABLE 1. Tabulation of eating disorder subtype by menstrual status[a,b]

	% (n)			
	AN ($n = 955$)	BN ($n = 292$)	ANBN ($n = 366$)	EDNOS ($n = 92$)
Normal	4.5 (43)	40.4 (118)	9.0 (33)	51.1 (47)
Oligomenorrhea	5.6 (53)	19.2 (56)	6.8 (25)	15.2 (14)
Secondary	77.7 (742)	35.6 (104)	77.1 (282)	30.4 (28)
Primary	12.2 (117)	4.8 (14)	7.1 (26)	3.3 (3)

Notes: AN, anorexia nervosa; BN, bulimia nervosa; ANBN, bulimia nervosa with history of anorexia nervosa; EDNOS, eating disorder not otherwise specified.

[a] Percents given are in reference to the eating disorder subtype.

[b] The eating disorder groups were not similarly distributed among the menstrual status groups (χ^2=457.39, df = 9, $p < .0001$). Specifically, the AN group was significantly different from the BN group ($p = .0003$) and the EDNOS group ($p = .0001$), and the ANBN group was significantly different from the EDNOS group ($p = .03$).

Frequency of Menstrual Disturbance Across Subtypes of EDs

Table 1 presents the results of the tabulation of eating disorder subtype by menstrual status. AN participants mostly reported secondary amenorrhea (77.7%). Among individuals with BN, those with a history of AN (ANBN) reported secondary amenorrhea more frequently than the other BN participants. Among the EDNOS participants, 3.3% reported primary amenorrhea, whereas 30.4% reported secondary amenorrhea. The eating disorder groups were not similarly distributed among the menstrual status groups ($\chi^2 = 457.39$, df = 9, $p < .0001$). Specifically, the AN group was significantly different from the BN group ($p = .0003$) and the EDNOS group ($p = .0001$), and the ANBN group was significantly different from the EDNOS group ($p = .0310$).

Association Between Menstrual Dysfunction and Eating Disorder Behaviors

Table 2 presents the means of the lifetime lowest BMI, highest BMI, and the number of calories/day the participant would allow themselves during the time they were restricting the most by menstrual status group. Participants in the normal menstrual status group and in the primary amenorrhea groups reported the most extreme values for minimum and maximum lifetime BMI. The normal menstruation group had significantly higher values and the primary amenorrhea group had significantly lower values compared to all the other menstrual groups for these BMI measures (respectively, $\chi^2 = 247.57$, $p = .0002$, and $\chi^2 = 70.44$, $p = .0002$).

For the mean number of calories/day at the time of most restrictive eating, those in the secondary

TABLE 2. Means (Std) of lifetime lowest BMI, highest BMI and the number of calories/day the participant would allow themselves during the time they were restricting the most[a] and results from analysis of variance comparing menstrual status groups on BMI measures and caloric intake at time of greatest restriction[b]

	χ^2 (*p*-value) df = 3	Normal (n) *N* = 241	Oligomenorrhea (o) *N* = 148	Secondary (s) *N* = 1156	Primary (p) *N* = 160
BMI, max	70.44 (.0002)	24.7 (3.8) o, s, p	23.1 (3.3) n, p	22.2 (2.9) n, p	20.8 (3.0) n, o, s
BMI, min	247.57 (.0002)	18.6 (2.4) o, s, p	17.4 (2.3) n, s, p	14.6 (2.4) n, o, p	13.9 (2.8) n, o , s
Mean caloric intake	57.95 (.0002)	727.9 (354.4) o, s, p *N* = 197	619.0 (332.0) n, s *N* = 124	503.6 (335.9) n, o *N* = 1023	535.2 (368.2) n *N* = 140

[a] there are 221 participants for whom these data are missing. Of these, 133 report that they did not restrict their caloric intake; 10 additional participants had information missing for both questions. The other 78 are missing these data.

[b] The χ^2 and *p* values are from an analysis of variance with GEE corrections, predicting the BMI and caloric variables from menstrual status groups. Results from the post hoc tests indicating which groups are significantly different at the $p < .01$ are given. The abbreviation for the group is listed in the header of each column. The group heading the column is significantly different from the groups listed in the respective cells, e.g. For mean caloric intake, those in the primary amenorrhea group are significantly different from those in the normal menstruation group.

TABLE 3. Frequency of those who use various inappropriate compensatory behaviors and those who binge by menstrual status [% (*N*)][a], and results from chi-square analysis comparing the menstrual status groups on various eating disorder behaviors[b]

	χ^2 (*p*-value) df = 3	Normal (n) *N* = 241	Oligomenorrhea (o) *N* = 148	Secondary (s) *N* = 1156	Primary (*p*) *N* = 160
Bingeing	66.72 (.0002)	68.9 (166) s, p	61.5 (91) s, p	42.2 (486) n, o	33.8 (54) n, o
Fasting	9.40 (.032)	49.2 (118) —	60.5 (89) —	55.0 (636) —	46.9 (75) —
Exercise	69.93 (.0002)	19.9 (48) s, p	25.0 (37) s, p	45.4 (525) n, o	39.4 (63) n, o
Appetite suppressants	28.73 (.0002)	44.0 (106) s, p	40.5 (60) p	32.1 (371) n	18.8 (30) n, o
Vomiting	48.14 (.0002)	73.0 (176) s, p	66.2 (98) s, p	53.1 (613) n, o	41.2 (66) n, o
Enemas	5.34 (.161)	5.8 (14) —	2.7 (4) —	6.3 (7) —	5.6 (9) —
Ipecac	1.89 (.595)	7.1 (17) —	6.8 (10) —	8.1 (93) —	5.6 (9) —
Diuretics	7.01 (.084)	14.1 (34) —	18.2 (27) —	15.7 (181) —	9.4 (15) —
Laxatives	9.65 (.031)	33.2 (80) s	40.1 (59) —	42.1 (486) n	34.4 (55) —
Any purging	39.39 (.0002)	80.5 (194) s, p	76.9 (113) s, p	64.7 (743) n, o	55.6 (89) n, o

[a] For fasting, vomiting, enemas, ipecac, diuretics, laxatives, fasting, and appetite suppressants, positive endorsement was considered a 1, 2, 3, or 4 on the respective SIAB items. For exercise, only a response of 4 was considered as positive endorsement. If the individual endorsed any of the purging methods (vomiting, enemas, ipecac, diuretics, and laxatives) with a 1, 2, 3, or 4, then they were considered as purgers (any purging).

[b] The χ^2 and *p* values are from logistic regression with GEE corrections, predicting the various eating behaviors from menstrual status groups. Results from the post hoc tests indicating which groups are significantly different at the $p < .01$ are given. The abbreviation for the group is listed in the header of each column. The group heading the column is significantly different from the groups listed in the respective cells, e.g., For exercise, those in the oligomenorrhea group are significantly different from those in the secondary and primary amenorrhea groups.

amenorrhea group reported the greatest caloric restriction and differed significantly from those in the normal menstruation and oligomenorrhea groups. Those in the normal menstruation group reported the least caloric restriction and differed significantly from the oligomenorrhea, secondary, and primary amenorrhea groups.

Table 3 presents the frequencies and the statistical comparisons of binge eating and the use of various inappropriate compensatory behaviors by menstrual status. Results from the post hoc analysis indicate which groups differed significantly at the $p < .01$ level.

For binge eating behavior, those in the normal menstruation and oligomenorrhea groups reported the highest frequency of binge eating, differing significantly from those in the secondary and primary amenorrhea groups. This is to be expected because women with BN who are of normal weight, by definition, binge. For vomiting, results were similar: those in the normal menstruation and oligomenorrhea groups reported the highest frequency of

vomiting, differing significantly from those in the secondary and primary amenorrhea groups. For excessive exercise, those in the primary and secondary amenorrhea groups reported the highest frequency and differed significantly from those in the normal menstruation and oligomenorrhea groups.

For the use of appetite suppressants, those in the primary amenorrhea group reported the lowest frequency of use, differing significantly from the normal menstruation and the oligomenorrhea groups. Those in the normal menstruation group reported the highest frequency of use and differed significantly from those in the secondary and primary amenorrhea groups.

For laxatives, the secondary amenorrhea group reported the highest frequency of use, and differed significantly from the normal menstrual status group. As for any purging behavior, the normal menstruation and oligomenorrhea groups reported the highest frequency and were significantly different from the secondary and primary amenorrhea groups.

The frequency of fasting and other purging behaviors including the use of ipecac, diuretics, and enemas did not show consistent significant differences across menstrual status groups.

Association Between Menstrual Dysfunction and AXIS I and II Disorders

For the Axis I and II disorders no significant differences were observed across the four menstrual status groups.

Association Among Menstrual Dysfunction, Personality, and Psychological Features

The analysis of variance tests indicated that following variables were significantly associated with menstrual disturbance: age of onset ($p < .005$), trait anxiety ($p < .001$), harm avoidance ($p = .003$), novelty seeking ($p = .001$), persistence ($p < .001$), self-directedness ($p = .010$), concern over mistakes ($p < .001$), doubts about actions ($p < .001$), personal standards ($p < .001$), organization ($p < .015$), parental expectations ($p = .017$), worst rituals ($p < .001$), worst preoccupations ($p < .001$), and obsessions ($p < .001$).

When all significant personality variables were entered into a stepwise discriminant analysis, YBC-EDS worst rituals (partial R-square = .107; F-value = 60.26, $p < .001$), TCI novelty seeking (partial R-square = 0.016; F-value = 7.94, $p < .001$), TCI harm avoidance (partial R-square = .008; F-value = 4.24, $p = .005$), MPS personal standards (partial R-square = 0.009; F-value = 4.29, $p = .005$), and YBOCS obsessions (partial R-square = .012; F-value = 5.70, $p < .001$) remained in the model.

On the YBC-EDS, significant lower scores for eating disorder rituals at the worst point of illness was reported by the normal menstruation group when compared with all other three menstrual status groups; also, the oligomenorrhea group showed significantly lower scores for worst rituals compared with the secondary and primary amenorrhea groups.

On the TCI, the oligomenorrhea and the secondary amenorrhea groups reported significantly higher scores on harm avoidance compared with the normal menstrual status group. For novelty seeking, the primary and secondary amenorrhea groups reported significantly lower scores than the normal menstrual status and oligomenorrhea groups.

On the MPS, significantly lower personal standards were reported by the normal menstruation group compared with the secondary and primary amenorrhea groups.

For the Y-BOCS, the oligomenorrhea and secondary amenorrhea groups reported the highest scores on obsessions, and were significantly different from the primary amenorrhea group. In addition, the secondary amenorrhea group had significantly higher scores on obsessions than the normal menstruation group.

Conclusion

The present study examined diagnostic, clinical, and nutritional variables, as well as personality traits and psychiatric comorbidity associated with menstrual disturbance in the largest and most diagnostically diverse cohort of eating disorder patients studied to date.

Overall, most AN participants reported secondary amenorrhea, but it is of note that ~18% of this diagnostic group reported other degrees of menstrual disturbance. Among the BN participants, 35.6% reported secondary amenorrhea. Those BN participants with a history of AN reported the highest frequency of secondary amenorrhea among the BN group (77.1%), in accordance with the findings of Copeland and Herzog.[17]

These findings illustrate that individuals with variants of AN and BN present with amenorrhea, oligomenorrhea, and normal menstrual function suggesting that menstrual status might not be an informative criterion to distinguish among ED subtypes. Other studies have shown that amenorrhea

did not discriminate between women with AN and women who met all diagnostic criteria except amenorrhea across a number of relevant variables such as demographics, illness characteristics, psychiatric comorbidity, and family history.[3,14,15,33–36]

The most relevant factors associated with menstrual dysfunction measured in this study were BMI, recalled caloric intake, and levels of exercise. Lifetime minimum BMI was significantly associated with amenorrhea as participants with primary amenorrhea reported the lowest maximum lifetime BMI and the lowest minimum lifetime BMI of all menstrual status groups. The normal menstrual status group reported the opposite profile-the highest maximum lifetime BMI and highest minimum lifetime BMI. The most severe caloric restriction during the acute phase of illness was reported by those with primary or secondary amenorrhea. Although these data are retrospective and subject to recall bias, they nonetheless suggest that low BMI and severe caloric restriction are significantly associated with menstrual dysfunction.

These findings concur with those of Copeland et al.,[61] who, in a longitudinal study of amenorrhea in ED, observed that those AN and BN patients with amenorrhea had a significantly lower mean percent ideal body weight. Factors other than weight loss may also contribute to amenorrhea in ED. The caloric restriction reported by the participants might reflect a diet with a lack of nutrients that are relevant to maintenance of the menstrual cycle. Gendall et al.[36] compared AN women with and without amenorrhea and found that percent energy from dietary fat was slightly but not significantly lower in women with amenorrhea. The nutrient composition analysis showed that there were also trends for greater intake of water, fiber, and percent energy protein and polyunsaturated fatty acids in women with amenorrhea compared to women without amenorrhea.

Those individuals with secondary amenorrhea reported the highest frequency of exercise, followed by the primary amenorrhea group. Reproductive dysfunction in exercisers can be attributed to the diversity of sports practice, the issue of overtraining, and inadequate energy balance. Exercise itself may have no deleterious effect on the reproductive system beyond the impact of its cost on energy availability.[62]

Although exploratory in nature, the present investigation also examined whether abnormal eating and weight control behaviors other than low body weight and energy intake were associated with menstrual dysfunction. Binge eating behavior, vomiting, and the use of appetite suppressants were significantly more frequent among individuals who reported normal menstruation and oligomenorrhea. The association of binge eating and normal menstruation and oligomenorrhea may be related to the fact that, when engaging in binge eating, at least a certain proportion of calories are being absorbed, which might be sufficient to maintain the menstrual cycle to some extent. Conversely, both binge eating and vomiting may also influence regulation of menses once they interfere with insulin response, leading to hyperandrogenism and polycystic ovary syndrome in some patients.[24,29] Also, a high frequency of vomiting may increase dopaminergic and opioid activity which has been implicated in menstrual irregularity.[31] Finally, appetite suppressants, especially amphetamines, can cause an increase in prolactin levels, leading to menstrual dysfunction.[63]

Patterns of comorbitidy and personality features yielded few distinguishing differences across menstrual status groups. We observed no differences across menstrual groups in terms of Axis I and II comorbid psychiatric disorders. These observations are consistent with previous studies that used smaller samples.[3,15,33–36,64] For example, Garfinkel et al.[3] found no differences in psychiatric comorbidity (major depression, anxiety disorders, and alcohol dependence) when women with AN with and without amenorrhea were compared. Other authors reported similar depression scores and general psychopathology among females with typical and atypical AN.[33,35] In addition, Ricca et al.[64] observed similar STAI and depression scores among women with EDNOS and typical ED.

In addition, for the personality variables, the stepwise discriminant analysis showed that the character dimension of TCI, worst preoccupation and worst motivation to change (YBC-EDS), trait anxiety, compulsions (YBOCS), concern over mistakes, doubts about actions, organization, and parental criticism and expectations (MPS) did not discriminate among the four menstrual groups. In relation to the observed differences in personality features among menstrual status groups, TCI novelty seeking scores (NS) were significantly lower in women with primary and secondary amenorrhea than in those with normal menstruation and oligomenorrhea. Our findings are consistent with Gendall et al.[65] who reported that amenorrheic women with AN had significantly lower NS. On the MPS, women with menstrual disturbance displayed higher scores on personal standards when compared to women with normal menstruation. Giles and Berga[66] observed that women with functional hypothalamic amenorrhea (FHA, a condition that

resembles subthreshold AN) reported higher perfectionistic standards when compared with organic amenorrhea and eumenorrheic women. In terms of obsessionality, we also observed that women with menstrual disturbance had higher scores on worst rituals (YBC-EDS) and obsessions (YBOCS). Estrogen affects areas of the brain that are not primarily involved in reproduction such as cognition and mood. It modulates serotonergic function via a variety of mechanisms including serotonin (5HT) receptor number and 5HT synthesis and metabolism.[67] Disrupted plasma levels of estradiol could also contribute to serotonergic dysregulation observed in women with AN and BN. Alterations in brain 5HT function are thought to contribute to diverse aspects of ED, including perfectionism, obsessionality, behavioral constraint, impulsivity, anxiety and mood regulation.[68,69]

In contrast, although we know that many of the psychological symptoms reported by individuals with ED can be the result of malnutrition, and that ovarian steroids have a considerable effect in pathways that regulate affect, cognition, and modulate 5-HT function,[70] the extent to which those factors differentially influence state and trait characteristics in ED, including personality features, remains unclear. The few psychopathological distinctions observed among the menstrual status groups may imply that some of the psychological features of ED are not only a direct consequence of nutrition deprivation and low levels of gonadal hormones (state related) but rather reflect core aspects of these disorders.

This study was designed to describe the landscape of menstrual status across subtypes of AN, BN, and EDNOS. The results reported here should be interpreted within the context of some limitations. As this is a cross-sectional study, the associations reported among the clinical and nutritional variables and menstrual status do not necessarily express a cause-effect relationship. In addition, all the clinical and nutritional measures were determined by self-report and thus subject to recall bias. There were no objective measures such as plasma concentrations of sex steroids and other hormones that are known to reflect reproductive function. Most of the neuroendocrine and neurotransmitter abnormalities that might explain some of the psychobiological disturbances observed in AN and BN, are, for the most part, state-related and tend to normalize after symptom remission [although there is some indication that serotonin activity alteration is a trait-related characteristic[69]]. Finally, participants included in this sample were originally recruited for a series of genetic studies and may not be representative of community or clinical samples with ED, and no comparative data with a noneating disorder group was available for the present report.

Despite these limitations, this study obtained information from a large cohort of participants enabling the examination of several clinical variables that may interact and influence menstrual status in women with ED.

Although the results of the present study are not surprising, they validate with new and extensive data that of all eating disorder behaviors we measured, BMI, low caloric intake, and levels of exercise show the strongest association with menstrual dysfunction. In addition, women with ED, irrespective of menstrual status, experience similar degrees of psychological distress, and no distinguishing Axis I and II comorbid disorders.

In summary, our findings suggest that varying levels of menstrual dysfunction are highly prevalent across all ED subtypes. Menstrual disturbance is an important clinical feature associated with serious and damaging eating disorder symptoms rather than a criterion that discriminates ED subtypes. When seeing a patient with any type of menstrual dysfunction, health care providers should remain alert and screen for ED, not just AN, but BN and EDNOS as well.

Taken together our results support reconsideration of amenorrhea as a diagnostic criterion for AN. Our recommendation is that the criterion be reconceptualized as an associated feature of AN, BN, and EDNOS with a broader indication of menstrual irregularity rather than amenorrhea of a specified and arbitrary duration.

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