ORIGINAL ARTICLE

Risk Factors for Anorexia Nervosa

Three Integrated Case-Control Comparisons

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Background: Many risk factors have been implicated in the development of anorexia nervosa. Little is known about their relative contributions, nor in most cases is it clear whether they are specific to anorexia nervosa or risk factors for all eating disorders or for psychiatric disorder in general.

Methods: We used a case-control design involving the comparison of 67 female subjects with a history of anorexia nervosa with 204 healthy control subjects, 102 subjects with other psychiatric disorders, and 102 subjects with bulimia nervosa. A broad range of risk factors was assessed by interview.

Results: The subjects with anorexia nervosa and the healthy controls differed in their exposure to most of the putative risk factors. There was no greater exposure to factors that increased the likelihood of dieting, once the influence of other classes of risk factors had been taken into account. Premorbid perfectionism and negative self-evaluation were especially common and more so than among the general psychiatric controls. Parental obesity and an early menarche, together with parental psychiatric disorder, distinguished those with bulimia nervosa from those with anorexia nervosa.

Conclusions: There appears to be a broad range of risk factors for anorexia nervosa and bulimia nervosa, some of which are shared with other psychiatric disorders. Factors that increase the likelihood of dieting seem to have more important influence as risk factors for bulimia nervosa than anorexia nervosa. Perfectionism and negative self-evaluation appear to be particularly common and characteristic antecedents of both eating disorders.

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MANY RISK factors have been implicated in the development of anorexia nervosa. These include a family history of anorexia nervosa,[1-3] obesity,[4] eating and weight concerns,[5] affective disorder,[1,6-12] substance abuse,[9,10,11,13] and obsessive-compulsive disorder[11,12,14]; a history of exposure to adverse events and circumstances[15-18]; and the presence of certain traits such as perfectionism, obsessionality, excessive compliance, and low self-esteem.[3,4,12,19] The research findings are difficult to interpret, because most studies have focused on a restricted range of putative etiologic factors; most samples have been recruited from specialist centers; and few studies have included general psychiatric control groups or control groups with other eating disorders.

We herein report the findings of a study of risk factors for anorexia nervosa. It complements and extends our studies of risk factors for bulimia nervosa[20] and binge eating disorder.[21] The study had the following 3 main aims: to identify risk factors for the development of anorexia nervosa; to determine which of these risk factors are especially common among subjects with anorexia nervosa compared with subjects with other psychiatric disorders; and to compare risk factors for anorexia nervosa with those for bulimia nervosa. Our study was designed to test the hypothesis that, as for bulimia nervosa,[20] there are 2 broad classes of risk factors for anorexia nervosa, those that increase the risk for psychiatric disorder in general and those that increase the risk for dieting. We also predicted on the basis of clinical observations and previous research that, whereas the risk factors for anorexia nervosa and bulimia nervosa would overlap substantially, a family and personal history of obesity and a family history of substance abuse would be less common among those with anorexia nervosa, whereas premorbid perfectionism would be more common.

SUBJECTS AND METHODS

DESIGN AND RECRUITMENT

A case-control design was used with 3 related comparisons, corresponding to the 3 main aims. Sixty-seven subjects with a history of anorexia nervosa were compared with 204 subjects without an eating disorder (healthy control subjects), 102 subjects with other psychiatric disorders (general psychiatric controls), and 102 subjects with bulimia nervosa.

The method used to recruit the 3 comparison groups and 12 of the subjects with anorexia nervosa is described in detail elsewhere.[20] All women aged from 16 to 35 years listed on 23 general practice patient registers in Oxfordshire, England, were sent 2 case-finding instruments, the Eating Disorder Examination-Questionnaire[22-24] and the 30-item General Health Questionnaire.[25] Respondents were interviewed if their responses suggested that they might be eligible for the study. The Eating Disorder Examination[26-28] and the Structured Clinical Interview for *DSM-III-R*[29,30] were used to establish diagnostic status. The 2 control groups with no eating disorder were individually matched to the subjects with bulimia nervosa in terms of age and parental social class, although there was group matching for the present comparisons. Both control groups were required to have no present or past eating disorder.

An additional 55 subjects with a history of anorexia nervosa were recruited from a National Health Service database that provided the names of all female patients with the diagnosis of anorexia nervosa seen by the psychiatric services in Oxfordshire from January 1, 1989, to December 31, 1994. Case notes for each patient were checked to corroborate the diagnosis. Ninety-three subjects met these criteria. Each subject's current general practitioner was contacted to see whether there was any reason why the patient should not be contacted. Seven were excluded as a result. Recruitment letters were written to the last known address of the others, 22 of whom did not reply and 9 of whom declined to be interviewed. The remainder underwent assessment in the same way as the other subjects. Few currently had anorexia nervosa. Informed consent was obtained from all subjects.

RISK FACTOR ASSESSMENT

Exposure to putative risk factors for eating disorders was assessed by interviewing the subjects (usually at their homes). Details of the assessment procedure are provided in our related article on bulimia nervosa[20] and an article on sexual abuse.[31] In the case of subjects with eating disorders, the interview focused on the period before its onset, with onset being conservatively defined as the age at which the first significant and persistent behavior characteristic of an eating disorder began.[20] This was to ensure that the exposures preceded the development of the eating disorder. The presence of 5 risk factors was assessed before and after onset, since they might have a hereditary influence (**Table 1**). The subjects also completed the Parental Bonding Instrument.[32] There were no additional informants. The risk factor interviews with the subjects with no eating disorder focused on the period before the age at onset of a matched case of bulimia nervosa,[20] but for the present study, there was group matching. The risk factor interview used behavioral definitions of key concepts[20] to minimize the problems associated with retrospective reporting.[33] (A copy of the schedule may be obtained by writing to one of us [C.G.F.].) A wide range of putative risk factors was assessed, and these were categorized a priori into domains and subdomains, each reflecting certain types of exposure (Table 1). Age at onset of menstruation was treated as a separate domain.

DATA ANALYSIS

The 3 sets of case-control comparisons used logistic regression analyses appropriate for an unmatched case-control design.[34,35] The analyses were undertaken after adjusting for current age, parental social class,[36] and age at onset of the eating disorder. Adjusting for current age reduced the risk for age-related recall bias, adjusting for parental social class removed a potential confounding variable, and adjusting for age at onset minimized differences in the time available for exposure. The relationships between individual putative risk factors and case status were assessed individually. Each risk factor was considered as a single indicator variable and coded 0 for no and 1 for yes. Statistical significance was assessed using the χ^2 likelihood ratio statistic and was set at the 1% level ($P<.01$) to achieve levels of statistical power comparable with those in the bulimia nervosa case-control study.[20] An overall measure of exposure to risk in each subdomain and domain was obtained by summing the number of component factors to which each subject had been exposed. The resulting index scores were grouped for the purposes of analysis into categories of as equal size as possible, with varying numbers for the subdomains and 4 for the domains. The relationships between case status and exposure in each subdomain and domain were first examined individually and then, to assess the relative importance of different types of exposure, in multiple stepwise logistic regression analyses. To test for the significance of any apparent linear trend, the categorized scores (each assigned a value of average exposure) were entered in factored and unfactored forms. Statistical significance for the subdomain and domain analyses was set at the 5% level ($P<.05$). Unless otherwise indicated, data are given as mean ± SD.

RESULTS

CHARACTERISTICS OF THE 4 SUBJECT GROUPS

The 67 subjects with anorexia nervosa had a mean age of 22.4 ± 4.8 years; mean age at onset of the eating disorder was 14.6 ± 3.0 years. The equivalent figures for the subjects with bulimia nervosa were 23.7 ± 4.9 years ($t_{167} = 1.77$ [$P = .08$]) and 15.5 ± 3.9 years, respectively ($t_{163} = 1.72$ [$P = .09$]). The subjects with anorexia nervosa had a significantly higher parental social class distribution than the subjects with bulimia nervosa

Table 1. Distribution of Putative Risk Factors in the 4 Subject Groups and Results of Univariate Regression Analyses*

	Subject Groups, No. (%)				Comparison With Subjects With Anorexia Nervosa					
					Healthy Controls		General Psychiatric Controls		Bulimia Nervosa Controls	
	With Anorexia Nervosa (n = 67)	Healthy Controls (n = 204)	General Psychiatric Controls (n = 102)	Bulimia Nervosa Controls (n = 102)	Odds Ratio (95% CI)	χ^2 *P*	Odds Ratio (95% CI)	χ^2 *P*	Odds Ratio (95% CI)	χ^2 *P*
Personal Vulnerability Domain										
Subdomain 1 (childhood characteristics)										
Negative self-evaluation	35 (55)	27 (13)	31 (30)	55 (54)	8.2 (4.2-16.1)	<.001	3.1 (1.7-6.3)	<.001	1.1 (0.6-2.2)	.70
Perfectionism	39 (61)	49 (24)	26 (26)	42 (42)	3.9 (2.1-7.4)	<.001	4.1 (2.0-8.3)	<.001	2.2 (1.1-4.5)	.03
Extreme compliance	20 (30)	42 (21)	27 (27)	29 (29)	1.6 (0.8-3.1)	.15	1.0 (0.5-2.1)	.96	1.0 (0.5-2.2)	.91
No close friends	13 (20)	10 (5)	10 (10)	18 (18)	5.6 (2.2-14.4)	<.001	3.0 (1.1-8.1)	.02	1.5 (0.6-3.4)	.39
School absence through anxiety	3 (5)	4 (2)	4 (4)	8 (8)	2.3 (0.5-11.4)	.32	0.8 (0.2-4.2)	.83	0.5 (0.1-2.2)	.38
Subdomain 2 (premorbid psychiatric disorder)										
Major depression	13 (21)	9 (4)	17 (17)	30 (29)	8.5 (3.0-24.0)	<.001	1.7 (0.7-4.2)	.25	0.7 (0.3-1.6)	.40
Drug abuse	4 (6)	1 (<1)	3 (3)	3 (3)	16.7 (1.7-161.0)	.005	2.7 (0.5-13.4)	.22	2.5 (0.4-13.9)	.30
Alcohol abuse	7 (13)	19 (10)	14 (14)	13 (13)	2.1 (0.7-6.0)	.19	1.2 (0.4-3.5)	.79	1.7 (0.5-5.8)	.39
Subdomain 3 (behavioral problems)										
Marked conduct problems	7 (11)	4 (2)	7 (7)	16 (16)	5.1 (1.4-18.5)	.01	1.5 (0.5-4.9)	.47	0.5 (0.2-1.5)	.23
School absence (truancy)	4 (6)	7 (4)	7 (7)	16 (16)	2.5 (0.7-9.4)	.19	1.3 (0.3-5.1)	.69	0.4 (0.1-1.3)	.11
Deliberate self-harm	7 (11)	2 (1)	9 (9)	13 (13)	17.1 (3.1-94.4)	<.001	1.4 (0.5-4.2)	.54	0.7 (0.3-2.1)	.58
Subdomain 4 (parental psychiatric disorder [ever])										
Parental depression (ever)	23 (34)	23 (11)	36 (35)	35 (34)	4.1 (2.0-8.2)	<.001	0.9 (0.5-1.7)	.73	1.1 (0.6-2.3)	.72
Parental alcoholism (ever)	6 (9)	8 (4)	7 (7)	24 (24)	2.6 (0.8-8.5)	.12	2.1 (0.6-7.7)	.26	0.4 (0.1-1.1)	.06
Parental drug abuse (ever)	1 (2)	1 (<1)	3 (3)	9 (9)	1.6 (0.1-26.5)	.76	0.5 (0.04-5.6)	.55	0.2 (0.02-1.46)	.050
Environmental Domain										
Subdomain 1 (parental problems)										
Low parental contact	20 (32)	36 (18)	14 (14)	34 (33)	1.8 (0.9-3.5)	.09	2.7 (1.2-6.1)	.02	0.8 (0.4-1.7)	.56
Separation from parents	8 (15)	9 (5)	10 (10)	13 (13)	4.8 (1.6-14.7)	.007	1.7 (0.6-4.8)	.34	1.2 (0.4-3.4)	.75
Parental										
Arguments	31 (46)	52 (26)	36 (35)	58 (57)	2.6 (1.4-4.7)	.002	1.8 (0.9-3.6)	.08	0.6 (0.3-1.3)	.18
Criticism	12 (18)	11 (5)	17 (17)	34 (33)	5.5 (2.1-14.3)	<.001	1.2 (0.5-2.7)	.71	0.4 (0.2-0.9)	.03
High expectations	30 (46)	43 (21)	25 (25)	51 (50)	2.5 (1.3-4.6)	.005	2.2 (1.1-4.5)	.03	0.7 (0.4-1.3)	.24
Overinvolvement	6 (9)	6 (3)	7 (7)	15 (15)	5.4 (1.4-19.9)	.013	1.7 (0.5-5.5)	.40	0.6 (0.2-1.6)	.27
Underinvolvement	40 (60)	70 (34)	43 (42)	59 (58)	3.6 (1.9-6.6)	<.001	2.1 (1.1-4.1)	.03	1.2 (0.6-2.3)	.60
Minimal affection	17 (26)	17 (8)	28 (28)	41 (40)	4.7 (2.1-10.6)	<.001	1.0 (0.5-2.2)	.93	0.6 (0.3-1.2)	.14
PBI (low care and high overprotection)										
Maternal	30 (51)	44 (23)	39 (46)	55 (63)	3.5 (1.8-6.7)	<.001	1.2 (0.6-2.4)	.58	0.5 (0.3-1.1)	.09
Paternal	29 (49)	54 (28)	41 (49)	44 (52)	2.9 (1.5-5.4)	.001	1.1 (0.5-2.2)	.79	0.9 (0.5-1.9)	.84
Subdomain 2 (disruptive events)										
Parental death	2 (3)	3 (2)	5 (5)	2 (2)	2.3 (0.3-16.3)	.41	0.7 (0.1-4.2)	.74	1.8 (0.2-14.0)	.59
Change of parent figure	14 (21)	23 (11)	20 (20)	18 (18)	2.5 (1.1-5.5)	.03	1.1 (0.5-2.5)	.79	1.4 (0.6-3.2)	.48
Parental chronic illness	13 (19)	40 (20)	36 (35)	28 (28)	1.1 (0.5-2.3)	.79	0.5 (0.2-0.98)	.04	0.7 (0.3-1.6)	.40
Frequent house moves	21 (31)	25 (12)	19 (19)	22 (22)	3.6 (1.8-7.5)	<.001	2.6 (1.2-5.7)	.02	1.9 (0.9-3.9)	.11
Severe personal health problems	9 (13)	7 (3)	14 (14)	12 (12)	5.0 (1.6-15.5)	.004	0.9 (0.3-2.4)	.85	1.4 (0.5-3.7)	.54
Subdomain 3 (parental psychiatric disorder)										
Parental depression	5 (8)	6 (3)	9 (9)	19 (19)	3.5 (0.9-13.0)	.07	0.8 (0.2-2.6)	.68	0.3 (0.1-1.0)	.04
Parental alcoholism	4 (6)	5 (3)	6 (6)	20 (20)	2.6 (0.6-11.2)	.20	1.2 (0.3-5.0)	.77	0.3 (0.1-1.0)	.04
Parental drug abuse	1 (2)	1 (<1)	2 (2)	9 (9)	1.6 (0.1-26.5)	.76	0.7 (0.05-9.3)	.78	0.2 (0.02-1.4)	.05

Table 1. Distribution of Putative Risk Factors in the 4 Subject Groups and Results of Univariate Regression Analyses* (cont)

	Subject Group, No. (%)				Comparison With Subjects With Anorexia Nervosa					
					Healthy Controls		General Psychiatric Controls		Bulimia Nervosa Controls	
	With Anorexia Nervosa (n = 67)	Healthy Controls (n = 204)	General Psychiatric Controls (n = 102)	Bulimia Nervosa Controls (n = 102)	Odds Ratio (95% CI)	χ^2 *P*	Odds Ratio (95% CI)	χ^2 *P*	Odds Ratio (95% CI)	χ^2 *P*
Environmental Domain (cont)										
Subdomain 4 (teasing and bullying)										
Teasing (not concerning, shape, weight, eating, or appearance)	16 (24)	25 (12)	12 (12)	15 (15)	2.0 (1.0-4.2)	.06	2.2 (0.9-5.2)	.07	1.9 (0.8-4.4)	.14
Bullying	6 (9)	9 (4)	13 (13)	11 (11)	2.4 (0.8-7.5)	.13	1.0 (0.3-3.0)	>.99	1.6 (0.5-5.2)	.41
Subdomain 5 (sexual and physical abuse)										
Sexual abuse	18 (27)	22 (11)	26 (26)	36 (35)	3.4 (1.6-7.1)	.001	1.4 (0.7-3.0)	.37	0.8 (0.4-1.6)	.53
Repeated severe sexual abuse	3 (5)	1 (<1)	3 (3)	9 (9)	15.3 (1.5-159.0)	.01	1.9 (0.3-10.3)	.47	0.9 (0.2-3.9)	.91
Physical abuse	18 (27)	18 (9)	30 (29)	33 (32)	4.9 (2.2-10.8)	<.001	1.0 (0.5-2.1)	.96	0.9 (0.4-1.9)	.79
Repeated severe physical abuse	5 (8)	1 (<1)	10 (10)	8 (8)	14.9 (1.6-136.0)	.004	0.9 (0.3-2.8)	.79	1.1 (0.3-3.9)	.85
Repeated severe physical or severe sexual abuse	8 (12)	2 (1)	12 (12)	12 (12)	15.9 (3.1-80.8)	<.001	1.2 (0.4-3.5)	.68	1.6 (0.6-4.6)	.38
Dieting Vulnerability Domain										
Subdomain 1 (dieting risk)										
Family member dieting										
For any reason	40 (60)	74 (36)	44 (43)	64 (63)	2.5 (1.4-4.5)	.003	2.1 (1.1-4.1)	.03	0.8 (0.4-1.6)	.60
For shape or weight	29 (43)	54 (27)	37 (36)	50 (49)	2.1 (1.1-3.8)	.02	1.4 (0.7-2.8)	.30	0.8 (0.4-1.5)	.40
Critical comments by family about shape, weight, or eating	30 (45)	51 (25)	32 (31)	66 (65)	2.6 (1.4-4.7)	.002	2.1 (1.1-4.2)	.03	0.5 (0.2-0.9)	.02
Repeated comments by others about shape or weight	17 (25)	28 (14)	23 (23)	34 (33)	2.6 (1.3-5.4)	.01	1.6 (0.7-3.6)	.24	0.9 (0.4-1.8)	.70
Teasing about shape, weight, eating, or appearance	24 (36)	57 (28)	43 (42)	50 (49)	1.5 (0.8-2.8)	.18	0.7 (0.4-1.4)	.35	0.6 (0.3-1.3)	.20
Parental history of anorexia nervosa or bulimia nervosa	1 (2)	0 (0)	1 (1)	5 (5)	. . .	. . .	2.1 (0.1-39.7)	.62	0.5 (0.05-4.3)	.47
Parental obesity	7 (11)	23 (11)	20 (20)	34 (34)	0.9 (0.4-2.5)	.92	0.5 (0.2-1.3)	.13	0.3 (0.1-0.7)	.004
Childhood obesity	16 (24)	31 (15)	13 (13)	41 (40)	1.9 (0.9-3.9)	.08	2.9 (1.2-7.0)	.02	0.5 (0.2-1.1)	.07
Subdomain 2 (obesity risk)										
Childhood obesity	16 (24)	31 (15)	13 (13)	41 (40)	1.9 (0.9-3.9)	.08	2.9 (1.2-7.0)	.02	0.5 (0.2-1.1)	.07
Parental obesity (ever)	14 (22)	31 (15)	29 (29)	44 (44)	1.8 (0.8-3.9)	.13	0.8 (0.4-1.8)	.63	0.5 (0.2-1.0)	.06
Subdomain 3 (parental eating disorder)										
Parental history of anorexia nervosa or bulimia nervosa (ever)	4 (6)	1 (<1)	2 (2)	6 (6)	15.0 (1.5-155.0)	.009	4.1 (0.6-26.8)	.12	1.4 (0.4-5.6)	.63
Additional Risk Factor										
Age at menarche, y										
14-18	20 (33)	60 (30)	30 (30)	19 (19)	1.0		1.0		1.0	
13	18 (30)	70 (35)	35 (35)	28 (28)	0.8 (0.4-1.7)	.74	0.8 (0.3-1.7)	.80	0.5 (0.2-1.2)	.04
9-12	22 (37)	68 (34)	36 (36)	54 (54)	1.1 (0.5-2.2)		0.9 (0.4-2.0)		0.3 (0.1-0.8)	

**The analyses controlled for current age, index age, and parental social class. The statistical significance of the exposure (likelihood ratio statistic, χ^2), odds ratio, and 95% confidence intervals (CI) are given for each factor. All exposures, except those labeled (ever), predate the onset of the eating disorder. PBI indicates Parental Bonding Instrument; ellipses, not applicable. Subject numbers for each risk factor vary on account of missing data.*

(49 [73%] vs 47 [46%] in social classes I and II; 12 [18%] vs 46 [45%] in social class III; and 2 [3%] vs 9 [9%] in social classes IV or V; $\chi^2_3 = 18.9$ [$P<.001$]; social class data were missing for 4 subjects). The diagnoses of the general psychiatric controls fell into the following principal categories: 83 subjects (81%) had major depressive disorder; 1 subject (1%) had bipolar disorder; and 18 subjects (18%) had an anxiety disorder.

Table 2. Factors in Each Domain to Which the Subjects Were Exposed and Results of Regression Analyses*

Domain, No. of Factors	Subject Groups, No. (%)				Comparison With Healthy Control Subjects		
	With Anorexia Nervosa (n = 67)	Healthy Controls (n = 204)	General Psychiatric Controls (n = 102)	Bulimia Nervosa Controls (n = 102)	Odds Ratio (95% CI)	χ^2_3	*P*
Personal vulnerability						52.2	<.001
0	8 (12)	87 (43)	21 (21)	5 (5)	1.00		
1	10 (15)	63 (31)	27 (27)	18 (18)	1.55† (0.6-4.3)		
2	14 (21)	30 (15)	21 (21)	20 (20)	4.54† (1.7-12.2)		
3-9	35 (52)	24 (12)	33 (32)	59 (58)	16.7‡ (6.5-42.6)		
					χ^2 = 50.5, *P*<.001		
Environmental						46.6	<.001
0-1	8 (12)	73 (36)	20 (20)	8 (8)	1.00		
2-3	12 (18)	74 (36)	21 (21)	8 (8)	1.62 (0.6-4.3)		
4-5	16 (24)	35 (17)	24 (24)	25 (25)	5.02† (1.9-13.5)		
6-18	31 (46)	22 (11)	37 (36)	61 (60)	15.3‡ (5.8-40.7)		
					χ^2 = 45.5, *P*<.001		
Dieting vulnerability						20.3	<.001
0	5 (8)	59 (29)	16 (16)	4 (4)	1.00		
1-2	37 (55)	107 (53)	58 (57)	36 (35)	4.35† (1.6-12.1)		
3	15 (22)	25 (12)	13 (13)	20 (20)	7.67‡ (2.4-24.4)		
4-8	10 (15)	13 (6)	15 (15)	42 (41)	11.3‡ (3.1-41.0)		
					χ^2 = 17.4, *P*<.001		

*The likelihood ratio statistic, χ^2 (with 3 df) and its P value are given for each factored domain score, and the odds ratio and 95% confidence interval (CI) are given for each factored level. The χ^2 statistic for linear trend (with 1 df) and its P value are also given. Subject numbers for each risk factor vary on account of missing data.

†P<.01.

‡P<.001.

§P<.05.

The 4 subject groups differed significantly in terms of their mean age at menarche (1-way analysis of variance, $F_{3,456} = 7.00$ [$P<.001$]). Post hoc tests (Tukey) showed that whereas the mean age at menarche of the subjects with anorexia nervosa did not differ significantly from that of the healthy controls or the general psychiatric controls, the subjects with bulimia nervosa had a significantly earlier menarche than all 3 other groups (12.3 ± 1.4 years compared with 12.9 ± 1.6 years in the subjects with anorexia nervosa [$P = .03$]; 13.0 ± 1.4 years in the healthy controls [$P<.001$]; and 12.9 ± 1.3 years in the general psychiatric controls [$P = .003$]). Equivalent findings were obtained if these analyses were restricted to those subjects in whom the onset of disturbed eating postdated their menarche.

COMPARISON WITH THE HEALTHY CONTROLS (AIM 1)

Individual Risk Factors

In comparison with the healthy controls, subjects with anorexia nervosa reported greater levels of exposure (at least at $P<.01$) to 7 of the personal vulnerability factors and more than half of the environmental factors (Table 1). They also reported greater exposure to 3 of the dieting vulnerability factors.

Overall Level of Exposure to Each Subdomain

The subjects with anorexia nervosa reported a greater level of exposure than the healthy controls to all the subdomains other than obesity risk. In each case, the greater the exposure, the greater was the risk for developing anorexia nervosa. Five subdomains entered the multiple regression model, 2 from the personal vulnerability domain (childhood characteristics, $\chi^2_2 = 23.0$ [$P<.001$], and premorbid psychiatric disorder, $\chi^2_1 = 7.99$ [$P = .005$]) and 3 from the environmental domain (parental problems, $\chi^2_2 = 36.9$ [$P<.001$]; disruptive events, $\chi^2_1 = 4.83$ [$P = .03$]; and sexual and physical abuse, $\chi^2_1 = 3.93$ [$P = .05$]).

Overall Level of Exposure to Each Domain

The subjects with anorexia nervosa had a significantly greater level of exposure than the healthy controls to all 3 domains. The odds ratios increased, in a linear fashion, from those subjects exposed to the smallest number of factors to those exposed to the largest (**Table 2**). Two domains entered the multiple regression model, with exposure in the personal vulnerability domain entering first ($\chi^2_3 = 52.2$ [$P<.001$]), followed by exposure in the environmental domain ($\chi^2_3 = 17.5$ [$P<.001$]; goodness-of-fit, $\chi^2_{260} = 214.4$ [$P<.001$]). After adjusting for exposure in these 2 domains, the 2 groups did not differ sig-

Subjects With Anorexia Nervosa						
General Psychiatric Controls				Bulimia Nervosa Controls		
Odds Ratio (95% CI)	χ^2_3	*P*		Odds Ratio (95% CI)	χ^2_3	*P*
	10.1	.02			2.43	.49
1.00				1.00		
0.67 (0.2-2.2)				0.36 (0.1-1.6)		
1.31 (0.4-4.0)				0.36 (0.1-1.5)		
2.64 (1.0-7.3)				0.41 (0.1-1.4)		
$\chi^2 = 7.81$, $P = .005$				$\chi^2 = 0.64$, $P = .42$		
	4.32	.23			4.14	.25
1.00				1.00		
1.93 (0.6-6.2)				1.13 (0.3-4.7)		
2.02 (0.7-6.3)				0.47 (0.1-1.7)		
2.87§ (1.02-8.1)				0.48 (0.1-1.5)		
$\chi^2 = 3.91$, $P = .05$				$\chi^2 = 3.03$, $P = .08$		
	5.40	.15			7.43	.05
1.00				1.00		
1.84 (0.6-5.7)				0.70 (0.2-3.0)		
3.80§ (1.03-14.0)				0.51 (0.1-2.3)		
3.12 (0.8-12.3)				0.23 (0.1-1.1)		
$\chi^2 = 4.19$, $P = .04$				$\chi^2 = 7.05$, $P = .008$		

nificantly in their exposure to the dieting vulnerability domain (**Table 3**) or the additional domain of age at menarche ($\chi^2_3 = 5.01$ [$P = .17$]). There was no significant statistical interaction between the personal vulnerability and environmental domains, suggesting that the effect of exposure in any 1 domain did not depend on the degree of exposure in the other, and that the effect of combined exposures was additive.

COMPARISON WITH THE GENERAL PSYCHIATRIC CONTROLS (AIM 2)

Individual Risk Factors

The subjects with anorexia nervosa differed from the general psychiatric controls with respect to just 2 factors, negative self-evaluation and perfectionism, both from the personal vulnerability domain, with the level of exposure being higher among those with anorexia nervosa (Table 1).

Overall Level of Exposure to Each Subdomain

The 2 groups differed significantly with respect to their exposure to 3 of the 12 subdomains: 2 subdomains from the personal vulnerability domain (childhood characteristics and premorbid psychiatric disorder) and 1 subdomain from the environmental domain (parental problems). In each case, the subjects with anorexia nervosa had been exposed to a significantly greater extent than the general psychiatric controls. Only the subdomain of childhood characteristics entered the multiple regression model ($\chi^2_2 = 13.1$ [$P = .001$]).

Overall Level of Exposure to Each Domain

The 2 groups differed significantly with respect to their exposure to the personal vulnerability domain ($\chi^2_3 = 10.1$ [$P = .018$]; goodness-of-fit, $\chi^2_{161} = 201.1$ [$P < .001$]), with the greater the degree of exposure, the greater the risk for development of anorexia nervosa (χ^2_1 for linear trend = 7.81 [$P = .005$]). After adjusting for exposure in this domain, the other 2 domains and the additional domain of age at menarche did not have an independent relationship with case status (Tables 2 and 3).

COMPARISON WITH THE SUBJECTS WITH BULIMIA NERVOSA (AIM 3)

Individual Risk Factors

The only statistically significant difference between the 2 groups was with respect to parental obesity (before index age), with the subjects with anorexia nervosa having less exposure (Table 1).

Overall Level of Exposure to Each Subdomain

The 2 groups did not differ in their exposure to any of the personal vulnerability subdomains, and differed only with respect to 1 environmental subdomain, parental psychiatric disorder, exposure being lower among the subjects with anorexia nervosa. They did, however, differ with respect to 2 of the dieting vulnerability subdomains, dieting risk and obesity risk. The subjects with anorexia nervosa had lower levels of exposure. On multiple regression analysis, all 3 subdomains entered the model (dieting risk, $\chi^2_2 = 11.9$ [$P = .003$]; parental psychiatric disorder, $\chi^2_1 = 5.47$ [$P = .02$]; and obesity risk, $\chi^2_1 = 4.49$ [$P = .03$]).

Overall Level of Exposure in Each Domain

The 2 groups differed with respect to just 1 of the 3 domains, dieting vulnerability, the level of exposure being lower in those with anorexia nervosa ($\chi^2_3 = 7.43$ [$P = .05$]; goodness-of-fit, $\chi^2_{161} = 201.7$ [$P < .001$]). The odds ratios decreased, in a linear fashion ($\chi^2_1 = 7.05$ [$P = .008$]), from those subjects exposed to the smallest number of factors to those exposed to the greatest (Table 2). On multiple regression analysis, after adjusting for exposure in the dieting vulnerability domain, neither of the other domains had an independent relationship with case status (Table 3). The additional domain of age at menarche did, however, have an independent relationship with case status ($\chi^2_1 = 7.26$ [$P = .007$]). Subsequent analyses in which there was adjustment for age at menarche revealed little evidence of confounding.

Table 3. Results of Stepwise Regression Analyses*

	Comparison With Subjects With Anorexia Nervosa								
	Healthy Controls			General Psychiatric Controls			Bulimia Nervosa Controls		
Domain, No. of Factors	Odds Ratio (95% CI)	χ^2_3	*P*	Odds Ratio (95% CI)	χ^2_3	*P*	Odds Ratio (95% CI)	χ^2_3	*P*
Personal vulnerability		52.2	<.001		10.1	.02	. . .		
0	1.00			1.00					
1	1.41 (0.5-4.0)			0.67 (0.2-2.2)					
2	2.84 (1.0-8.3)			1.31 (0.4-4.0)					
3-9	8.74† (3.1-24.4)			2.64 (1.0-7.3)					
Environmental		17.5	<.001	. . .			. . .		
0-1	1.00								
2-3	1.01 (0.3-2.9)								
4-5	2.77 (1.0-8.1)								
6-18	5.79‡ (2.0-17.0)								
Dieting vulnerability	. . .			. . .				7.43	.05
0							1.00		
1-2							0.70 (0.2-3.0)		
3							0.51 (0.1-2.3)		
4-8							0.23 (0.1-1.11)		

**The significance of the exposure (likelihood ratio statistic, χ^2, with* df*), odds ratios, and 95% confidence intervals (CI) are given for each domain that had an independent relationship with case status (listed in order of entry to the regression model). Ellipses indicate that the variable did not enter the regression model.*

†P<*.001.*

‡P<*.01.*

COMMENT

RISK FACTORS FOR ANOREXIA NERVOSA AND BULIMIA NERVOSA

The findings of the comparison between the subjects with anorexia nervosa and the healthy controls support those of earlier etiologic studies in that the great majority of the putative risk factors were found to be risk factors for anorexia nervosa. This was true across all 3 domains, with there being clear dose-response effects. An unexpected finding was that only the personal vulnerability and environmental domains entered the multiple regression model. After adjusting for their influence, exposure in the dieting vulnerability domain no longer distinguished the groups.

The findings of the comparison between the subjects with anorexia nervosa and the general psychiatric controls were also contrary to the prediction concerning risk factors for dieting. There were no differences between the groups in their exposure to any of the dieting vulnerability factors or to the dieting vulnerability subdomains or domain. This result is quite unlike the findings of the comparable comparison involving subjects with bulimia nervosa,[20] where exposure to all 3 dieting vulnerability subdomains, and the domain as a whole, distinguished the 2 subject groups. Instead, the major difference between the 2 groups was with respect to the personal vulnerability domain and most especially the childhood characteristics subdomain. Within this subdomain, 2 childhood characteristics stood out, negative self-evaluation and perfectionism, both of which were substantially more common among the subjects with anorexia nervosa; indeed, they were the only individual factors that distinguished the 2 groups.

Three differences of note emerged from the comparison between the subjects with anorexia nervosa and those with bulimia nervosa. First, the 2 groups differed in their exposure to the dieting vulnerability domain as a whole, and to 2 of its 3 subdomains, with the rates being higher among those with bulimia nervosa. Examination of the exposure rates to individual dieting vulnerability factors revealed that among the subjects with bulimia nervosa, there was a higher rate of parental obesity (during the subject's own childhood) and an equivalent statistical trend with respect to frank childhood obesity ($P = .07$). This is in accord with previous findings.[4,37-39] There was also a trend for the subjects with bulimia nervosa to have received more negative comments from family members about their eating, appearance, or weight ($P = .02$). The second major finding was that age at menarche had an independent relationship with case status, which was not accounted for by childhood obesity, with the subjects with bulimia nervosa having an earlier menarche. The third finding, which arose from the subdomain analyses, was that the subjects with bulimia nervosa had been exposed to more parental psychiatric disorder during their childhood, with there being raised rates of parental depression, alcohol abuse, and drug abuse.

From the findings of these comparisons and those of the earlier study of bulimia nervosa,[20] it appears that in anorexia nervosa and bulimia nervosa, a major class of risk factor is a general one that is associated with increased risk for adult psychiatric disorder and depression in particular. It encompasses a broad range of adverse childhood experiences and raised rates of parental and childhood depression and deliberate self-harm. Unlike Schmidt et al,[16] we found no evidence of greater exposure to adverse childhood experiences among those with bulimia nervosa.

Exposure to these risk factors seems to be combined with exposure to 2 other classes of risk factor. The first consists of 2 psychological traits, negative self-evaluation and perfectionism, the latter being an especially common antecedent of anorexia nervosa. This finding converges with those of Rastam[4] and the Pittsburgh family study[12] in implicating perfectionism and possibly obsessive-compulsive personality disorder in the development of anorexia nervosa. The second class of distinctive risk factor seems to be one that directly encourages dieting. This is evident in anorexia nervosa, in that there are raised rates of parental eating disorders, family dieting, and adverse comments from family members about eating, appearance, or weight. On the other hand, these dieting vulnerability factors appear to have little influence once other risk factors are taken into account. In contrast, factors that promote dieting are extremely prominent in bulimia nervosa, and our previous findings suggest that they have an effect that is independent of other risk factors.[20] Three such factors appear to have a particularly important influence; namely, childhood obesity, parental obesity, and an early menarche. It seems that people in whom bulimia nervosa develops are vulnerable to be heavier than their peers, and that this vulnerability and its social consequences, together with having had obese parents and an early menarche, may sensitize them to their appearance and weight, and thereby encourage dieting.

One further class of risk factor appears relevant to bulimia nervosa. This is parental substance abuse, a finding that converges with those from family studies.[40] Clinical observations suggest that a subgroup of people with bulimia nervosa learn to modulate their mood by consuming large quantities of food, alcohol, or psychoactive drugs.

ISSUES OF METHOD

A strength of our 2 previous case-control studies[20,21] is that the subjects were recruited directly from the community. This recruitment method is impracticable in the case of anorexia nervosa due to the relative rarity of the disorder and its egosyntonic character. We therefore followed the suggestion of Walters and Kendler[3] by recruiting a representative sample of treated patients. These were secondary referrals from the same geographic area as the other subjects in the study. Although this sample should have been less affected by referral bias than samples from specialist clinics, it is still likely to have been subject to greater selection bias than our community samples; for example, it might be expected that these subjects' eating disorder would have been more severe.

In all other regards, the methods used in our study were identical to those used in our 2 earlier case-control studies.[20,21] Strengths include the broad range of putative risk factors assessed, the attention paid to temporal precedence of exposure, and the analysis of the relative contributions of the risk factors and their interaction. Limitations include reliance on retrospective report, nonblind assessment, and the absence of informants, each of which has been considered in the previous reports.[20,21,31] The choice of a mixed psychiatric control group was appropriate, given our aim to compare risk factors for specific eating disorders with those for psychiatric disorder in general. It was not possible to examine risk factors for subtypes of anorexia nervosa or bulimia nervosa because of the small subsamples involved. Similarly, no account was taken of movement across eating disorder categories over time, although subsequent 5-year annual follow-up of the subjects with bulimia nervosa and binge eating disorder has revealed little evidence of such movement. Overlap between the diagnostic categories would have tended to minimize the group differences observed rather than exaggerate them.

IMPLICATIONS FOR FUTURE RESEARCH

This series of case-control studies has identified various constitutional and environmental risk factors for the development of the 3 specific eating disorders recognized in *DSM-IV*.[41] The findings point to a need to extend etiologic research on eating disorders to focus on the interaction between genetic and environmental influences and the nature of the processes and mechanisms involved. The findings also suggest that family and childhood obesity, adverse childhood experiences, the traits of perfectionism and negative self-evaluation, and age at menarche merit more attention as risk factors than they have received to date.

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