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Is major depressive episode related to anxiety disorders in anorexics and bulimics?☆

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Abstract

Objective: To determine whether the presence of anxiety disorders is related to depressive comorbidity in subjects with eating disorders (ED), while taking into account certain variables that may be related to depression (subjects' age, ED duration, prior incidents of anorexia nervosa in bulimic subjects, inpatient or outpatient status, nutritional state [as measured by body mass index]).
Method: We evaluated the frequency of depressive disorders in 271 subjects presenting with a diagnosis of either anorexia nervosa or bulimia, using the Mini International Neuropsychiatric Interview, *DSM-IV* version.
Results: A multivariate analysis reveals that anxiety disorders do not all have the same influence in terms of risk of onset of major depressive episode in anorexics and bulimics when adjusted on variables related to depression.
Conclusion: Depression in subjects with ED can be explained in part by comorbidity with obsessive-compulsive disorder, generalized anxiety, social phobia, and panic disorder.

1. Introduction

Anxiety and depressive disorders are extremely frequent in subjects with eating disorders (ED). Lifetime prevalence of major depressive episode (MDE) is estimated between 50% and 71.3% in anorexics (AN) and approximately 61% in bulimics (BN) [1-5]. Lifetime prevalence of anxiety disorders is also substantial, varying from 33% to 72% in AN subjects and 41% to 75% in BN subjects [3,6-8].

Authors, such as Angst [9], have emphasized that "most depressed patients are anxious, and most anxious patients are depressed." Therefore, two thirds of depressed subjects demonstrate lifetime comorbidity with anxiety disorders over their lifetime, and, conversely, one third of patients diagnosed with anxiety disorders concomitantly develop depression. This is true for the general as well as the clinical population [10]. The (lifetime) comorbidity of MDE, the most common depressive disorder, is 20.3% with generalized anxiety disorder (GAD), 15.2% with simple phobia, 10.0% with panic disorder, 5% with agoraphobia, 4.1% with obsessive-compulsive disorder (OCD), 2% with simple phobia, and 0% with posttraumatic stress disorder [11]. In contrast, all types of anxiety disorders may be associated with depression and often are [12,13]. The comorbidity of anxiety disorders with MDE varies between 32% and 50% [14], that is, MDE is measured at 50% to 80% for panic disorder [15], 42% for GAD [16], 33.8% for simple phobia [17], and 28.77% for OCD [18]. Subjects presenting with a double diagnosis of depression and anxiety report that the anxiety disorder most often developed before the depressive disorder, particularly in cases of generalized anxiety [19].

☆ All authors disclose any financial conflict of interest.

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Comorbidity of depression with anxiety has rarely been studied in subjects with ED, although, as early as 1988, Hudson et al [4] posed the hypothesis that ED-anxiety comorbidity develops through comorbidity with depression. The connections between depression and anxiety disorders have not been examined in studies using the *DSM-III* because of diagnostic hierarchical criteria that favor the diagnosis of depression [11]; yet, only one study has looked into double comorbidity using *DSM-III-R* criteria, which showed that the presence of an anxiety disorder increases the risk of developing a depressive disorder by 3.6% in BN subjects [20]. We found no further data in the literature on this subject.

When studying the connection between anxiety and depression in subjects with ED, it is important to consider anxiety disorders as a whole. Indeed, in the clinical and general populations, specific anxiety disorders are frequently comorbid with other anxiety disorders [21], which holds true as well for subjects with ED: 66% of AN subjects and 50% of BN subjects manifest from 2 to 5 anxiety disorders in their lifetime [7].

We found no data in the literature regarding relative chronology of the onset of anxiety disorders and depressive disorders when they are comorbid in patients with ED. In light of the fact that anxiety disorders usually precede depression, we wondered about the impact of anxiety disorders on the development of a depressive disorder.

In previous studies, we have demonstrated that other factors may influence the comorbidity of ED and MDE, such as inpatient or outpatient status [22,23] or nutritional state [24]; in addition, the age of the subjects and duration of the disorder should be taken into account because, particularly in the case of young subjects, the likelihood of developing a disorder is related to age.

These considerations taken together prompted us to conduct a study with the primary objective of determining whether the presence of some or all anxiety disorders is related to depressive comorbidity in subjects with ED, while taking into account certain variables that may be related to depression (subjects' age, ED duration, prior incidents of anorexia nervosa in BN subjects, inpatient or outpatient status, nutritional state [as measured by body mass index or BMI]). Our secondary objective is to evaluate the relative chronology of the onset of anxiety disorders and depressive disorders in anorexic and bulimic subjects.

2. Methods and materials

2.1. Subjects

Young women seeking care for ED were recruited from within a multicentric study on addictive behaviors in France (Réseau INSERM Dépendance, n°494013) [25-27]. Included were women seen in either inpatient or outpatient settings; seen in one of the clinical centers within the network, with current *DSM-IV* diagnosis of AN or BN; and aged 15 to 30 years for AN patients and 15 to 40 years for BN patients. Exclusion criteria were presence of psychotic disorder; existence of chronic or severe physical illness having potential psychological effects or possibly influencing weight and eating (eg, diabetes); and inability to read questionnaires or understand French.

2.2. Ethical considerations

All subjects were recruited from within the Dependence Network system of the INSERM n°494013. The study received approval from the Consulting Committee for the Protection of Subjects in Biomedical Research (CCPPRB) through the Cochin-Port Royal hospital, Paris, France. All subjects were informed of study content and were given detailed consent forms, which they signed and returned to the researcher. Parents of minor patients and minor patients themselves agreed through informed and written consent. All data collected were anonymous (with the approval of the Commission Nationale Informatique et Liberté).

2.3. Instruments

A sociodemographic questionnaire was created for the study. To assess anxiety and depression as well as ED diagnosis, modules from a structured diagnostic interview were used: the Mini International Neuropsychiatric Interview (MINI), validated in French [28-30]. The MINI version 4.1 assesses *DSM-IV* Axis I psychiatric diagnostic criteria in a standardized fashion [31], with interrater reliability ranging from 0.88 to 1.0. All evaluators participating in this study received training in the use of the MINI by the authors of the instrument (E Weiller, INSERM U302, Paris, France).

The diagnoses assessed by the MINI in this study were the following: ED diagnosis (AN restrictive type [AN-R] or AN with purging [AN-BN]; BN with purging [including use of diuretics] [BN-P] or without purging [BN-NP]), anxiety disorders (panic attack disorder, agoraphobia, social phobia, OCD, GAD over the preceding 6 months, and posttraumatic stress disorder), and depressive disorders (MDE and dysthymia over the prior 2 years). For each disorder present, the MINI assesses age of onset and age of remission (age at which the subject initially presented disorders fulfilling diagnostic criteria; age at which the subject no longer presents symptoms fulfilling diagnostic criteria). We defined the presence of "at least one anxiety disorder" as the presence of 1 or more of the 6 anxiety disorders evaluated. Lifetime frequency defines subjects who currently manifest a disorder, or have in the past. Current disorders were defined as symptoms occurring in the preceding month, with the exception of GAD, which was evaluated over the preceding 6 months. Body mass index or Quetelet index (weight in kilograms divided by height in meters squared) was calculated to describe subjects' nutritional state [32].

3. Statistical analyses

3.1. Univariate analyses

Qualitative variables were described in percentages and proportions. Proportions were compared using χ^2 or Fisher exact test, depending on sample size [33]. Quantitative variables were described using the mean and standard deviation. The means were compared using Student t test (for variables with a normal curve distribution). All of these statistical tests are bilateral; based on the number of analyses we performed, our chosen level of significance was $\alpha = .01$.

3.2. Logistic regression

We undertook stepwise logistic regressions including, as the variable to explain, both lifetime MDE and current MDE. Explanatory variables initially introduced in the regressions were selected from two sources: data from the literature and clinical pertinence (according to the present authors). Their statistical significance (at the $P < .05$ level) in the univariate tests comparing their value as a function of the variable to be explained (social disability in two categories: disability or no disability) was also a criterion for selection.

In each case, to choose the best model of logistic regression, different models corresponding to all possible explanatory variables were tested to ensure appropriate adjustment and to maximize the percentage of subjects correctly classified by the model, using the method of maximum likelihood. Coefficients were estimated and their standard errors calculated. Variables were eliminated from the model based on likelihood ratio tests. Quality of adjustment was evaluated by χ^2 given through the regressions.

Separate analyses were conducted for anorexics and bulimics.

The SPSS 10 program was used to collect and analyze the data.

4. Results

4.1. Subject characteristics

The 271 subjects with ED were divided into 4 groups according to *DSM-IV* criteria: 111 AN-R, 55 AN-BN, 86 BN-P, and 19 BN-NP. The characteristics of each group are described in Table 1.

Regarding socioprofessional status, 82.9% of the AN-R group and 63.9% of the AN-BN group were students, whereas 57.9% of the BN-P group and 53.9% of the BN-NP group were employed. Most of the patients were unmarried (80.2% of the BN-NPs, 89.5% of the BN-Ps, 85.2% of the AN-BNs, and 98% of the AN-Rs); only a few had children (4 BN-NPs and 4 BN-Ps).

4.2. Clinical characteristics of the subjects

Given that there was no significant difference in terms of the presence of each anxiety disorder or MDE between the AN-Rs and AN-BNs and the BN-Ps and BN-NPs, we combined the subjects into an AN group and a BN group. The rates of (current and lifetime) existence observed for each anxiety disorder and each depressive disorder are shown in Table 2.

Table 2
Lifetime presence of anxiety disorders and MDE in anorexics and bulimics

	Anorexia nervosa (166)		Bulimia nervosa (105)	
	Number	Percentage	Number	Percentage
Lifetime disorder				
At least one anxiety disorder	118	71.1	67	63.7
Agoraphobia	37	22.29	18	17.14
Panic disorder	27	16.27	22	20.95
Social phobia	65	39.16	38	36.19
OCD	40[a]	24.10	11	10.48
MDE	126	75.90	79	75.24
Current disorder				
At least one anxiety disorder	104	62.6	63	60.0
Agoraphobia	27	16.27	11	10.48
Panic disorder	14	8.43	14	13.33
Social phobia	52	31.33	32	30.48
OCD	31[c]	18.67	8	7.62
Generalized anxiety (over 6 mo)	79[d]	47.59	33	31.43
Posttraumatic stress disorder	6	3.61	6	5.71
MDE	76[b]	45.78	34	32.38
Dysthymia (past 2 y)	13	7.83	16	15.24

Comparisons of AN vs BN: [a]$P = .01$; [b]$P = .03$; [c]$P = .014$; [d]$P = .009$.

Table 1
Group description of anorexics and bulimics

	Anorexia nervosa			Bulimia nervosa		
	AN	AN-R	AN-BN	BN	BN-P	BN-NP
Number	166	111	55	105	86	19
Age	19.74 ± 3.07[a]	19.31 ± 3.01[b]	20.60 ± 3.02	23.11 ± 5.01	22.78 ± 4.47	24.63 ± 6.91
ED duration	2.78 ± 2.42[a]	2.4 ± 2.05[b]	3.51 ± 2.89	5.64 ± 4.83	4.90 ± 4.96[c]	7.39 ± 7.53
BMI	15.12 ± 1.5[a]	14.87 ± 1.87[b]	15.64 ± 2.00	21.15 ± 3.85	20.34 ± 3.27[c]	24.77 ± 4.23

Values are expressed as mean ± SD unless otherwise indicated. AN-R indicates anorexia nervosa restrictive type; AN-BN, anorexia nervosa with bulimic episodes (vomiting or laxative abuse); BN-P, bulimia with purging; BN-NP, bulimia without purging.

[a] $P < .001$ in comparison with the BNs.

[b] $P < .01$ in comparison with the AN-BNs.

[c] $P < .01$ in comparison with the BN-NPs.

Table 3
Relative chronology of onset of anxiety disorders and MDE in anorexic and bulimic subjects

Anxiety disorders	No. of subjects with a lifetime diagnosis of MDE and anxiety disorder	Onset of anxiety disorder at least 1 y before onset of MDE N (%)
At least one anxiety disorder	100 AN	38 (38)
	56 BN	24 (42.9)
Agoraphobia	34 AN	11 (32.4)
	16 BN	3 (18.8)
Panic disorder	25 AN	5 (20)
	20 BN	4 (20)
Social phobia	55 AN	22 (40.0)
	32 BN	15 (46.9)
OCD	37 AN	11 (29.7)
	10 BN	5 (50)
Generalized anxiety	70 AN	11 (15.7)
	28 BN	7 (25)
Posttraumatic stress disorder	5 AN	2 (40)
	6 BN	2 (33)

Thus, 71% of the ANs and 64% of the BNs showed at least one lifetime anxiety disorder, and 75.9% of the ANs and 75.25% of the BNs showed a lifetime MDE. Most of the lifetime disorders present were still present at the time of evaluation.

The relative chronology of the onset of anxiety disorders and MDE is summarized in Table 3. One or more anxiety disorders precede MDE in approximately 40% of the cases, with significant variations from one disorder to another; the proportion of cases with an onset before MDE does not exceed 50% for any anxiety disorder.

4.3. Factors that influence the presence of MDE

We formulated the hypothesis that factors having a potential influence on (lifetime or current) MDE in subjects with ED are the following: anxiety disorders, subjects' age, duration of the ED, BMI, inpatient or outpatient status (with outpatient status coded as 0 and inpatient status as 1 for reference purposes), and prior existence of anorexia nervosa in BN subjects.

4.3.1. Determination of factors related to a lifetime diagnosis of MDE

4.3.1.1. Selection (through univariate analyses) of explanatory variables initially introduced in the logistic regression model. We searched for a possible association between each potential predictive factor, as defined above, and lifetime diagnosis of MDE in AN and BN subjects. We first considered "at least one anxiety disorder," then, in the second round, each disorder separately.

In anorexics, all lifetime anxiety disorders explored here, and GAD, are significantly related to MDE, represented by an increase in the prevalence of MDE in cases where an anxiety disorder is present (at least one anxiety disorder: 79.4% vs 29.0%, $P < .0001$; agoraphobia: 27% vs 7.5%, $P = .01$; panic disorder: 19.8% vs 5.0%, $P = .027$; social phobia: 43.7% vs 25%, $P = .035$; OCD: 29.4% vs 7.5%, $P = .05$; GAD: 55.6% vs 22.5%, $P = .0001$). However, there is no significant relationship between lifetime MDE and subjects' age, AN duration, BMI, or inpatient/outpatient status.

In bulimics, only lifetime diagnoses of "at least one anxiety disorder" and panic disorder and inpatient or outpatient status are significantly related to lifetime MDE, represented by an increase in the prevalence of MDE in cases where anxiety disorder is present (at least one anxiety disorder: 70.9% vs 42.3%, $P = .009$; panic disorder: 79.0% vs 26.0%, $P = .055$; inpatient/outpatient status: 70.9% vs 42.3%, $P = .009$).

All variables that were significantly related to depression were introduced in the initial logistic regression model.

4.3.1.2. Logistic regression. The final models obtained for anorexics are as follows:

1. A lifetime diagnosis of MDE is 4.7 times more frequent in the presence of "at least one lifetime anxiety disorder" ($P = .0001$; confidence interval [CI], 2.2-10.0); this model correctly classifies 75.9% of the observations.
2. For anxiety disorders in general, we found that panic disorder ($P = .075$), OCD ($P = .057$), and generalized anxiety ($P = .005$) explain a lifetime diagnosis of MDE; thus, MDE is 3.3 times more frequent in AN subjects with GAD (Table 4).

The final models obtained for bulimics are as follows:

1. A lifetime diagnosis of MDE is 2.8 times more frequent in the presence of at least one lifetime anxiety disorder ($P = .034$; CI, 1.1-7.3); subjects' inpatient or outpatient status is not significantly related to MDE; this model correctly classifies 74.8% of the observations.
2. No significant relationship is emphasized between any specific anxiety disorder and lifetime presence of MDE.

Table 4
Predictive factors of lifetime MDE in AN subjects: results of logistic regression

	P	OR	CI	% Of subjects correctly classified in the model
Lifetime panic disorder	.075	4.0	(0.9-18.5)	79.9
Lifetime OCD	.057	3.5	(0.7-16.4)	
Generalized anxiety (over 6 mo)	.005	3.3	(1.4-7.8)	

OR indicates odds ratio.

4.3.2. Determination of factors related to current MDE diagnosis

4.3.2.1. Selection (through univariate analyses) of explanatory variables initially introduced in the logistic regression model. We searched for a possible association between each potential predictive factor, as defined above, and a current diagnosis of MDE in anorexics and bulimics.

In AN subjects, all of the anxiety disorders explored here, with the exception of posttraumatic stress disorder, are significantly related to MDE, represented by an increase in the prevalence of MDE in cases where anxiety disorder is present (at least one anxiety disorder: 80.3% vs 47.8%, $P < .0001$; agoraphobia: 23.7% vs 10.0%, $P = .017$; panic disorder: 14.5% vs 3.3%, $P = .01$; social phobia: 46.1% vs 18.9%, $P = .0001$; OCD: 27.6% vs 11.1%, $P = .007$; GAD: 61.2% vs 35.6%, $P = .001$). However, there is no significant relationship between MDE and subjects' age, duration of AN, BMI, or inpatient/outpatient status.

In bulimics, each of the anxiety disorders explored here (with the exception of posttraumatic stress disorder and OCD), as well as inpatient/outpatient status, are significantly related to MDE represented by an increase in prevalence of MDE in cases where anxiety disorder is present (at least one anxiety disorder: 82.4% vs 50.0%, $P = .009$; agoraphobia: 20.6% vs 5.6%, $P = .036$; panic disorder: 29.4% vs 5.6%, $P = .002$; social phobia: 47.1% vs 22.5%, $P = .011$; GAD: 50.0% vs 22.5%, $P = .005$; inpatient/outpatient status: 44.1% vs 11.4%, $P = .0001$). However, there is no significant relationship between MDE and subjects' age, BN duration, BMI, or prior existence of AN. All variables significantly related to depression were introduced in the initial logistic regression model.

4.3.2.2. Stepwise logistic regression. The final models obtained for the anorexics are as follows:

1. A current diagnosis of MDE is 4.5 times more frequent in the presence of "at least one anxiety disorder" ($P = .0001$; CI, 2.2-9.0); this model correctly classifies 65.0% of the observations.
2. For anxiety disorders in general, MDE was found to be 3 times more frequent in the presence of a current diagnosis of social phobia and 2.4 times more frequent in the presence of a current diagnosis of GAD (Table 5).

Table 5
Predictive factors of current MDE in AN subjects: results of logistic regressions

	P	OR	CI	% Of subjects correctly classified in the model
Current social phobia	.003	3.0	(1.5-6.2)	65.1
Generalized anxiety (over 6 mo)	.011	2.4	(1.2-4.6)	

Table 6
Predictive factors of current MDE in BN subjects: results of logistic regression

	P	OR	CI	% Of subjects correctly classified in the model
Generalized anxiety (over 6 mo)	.037	4.2	(1.1-7.2)	78.8
Current panic disorder	.042	2.8	(1.1-16.6)	
Inpatient or outpatient status	.009	4.2	(1.2-4.6)	

The final models obtained for bulimics are as follows:

1. Current MDE is 3.3 times more frequent in the presence of "at least one current anxiety disorder" ($P = .034$; CI, 1.2-9.4), if we take into account subjects' inpatient/outpatient status, which increases the risk of MDE by a factor of 4.5 ($P = .004$; CI, 1.6-12.7); this model correctly classifies 78.8% of the observations.
2. Current MDE is 4.2 times more frequent in the presence of a current diagnosis of GAD and 2.8 times more frequent in the presence of a current diagnosis of panic disorder. Furthermore, MDE is 4.2 times more frequent in hospitalized patients than in outpatients (Table 6).

5. Discussion

Like many earlier studies, our results demonstrate the extremely high frequency of depressive disorders and anxiety disorders in subjects with ED. We also showed in an earlier study that the prevalence of most of these disorders was significantly higher than that of a control group [27]. Our results show, moreover, that the presence of "at least one anxiety disorder" increases the lifetime risk and present risk of major depression in anorexics as well as bulimics. The risk for anorexics of developing MDE in cases of comorbidity with at least one anxiety disorder is 4.7 times higher, and the risk for bulimics is approximately 3 times higher. This result supports the only other study that has evaluated this risk (in a clinical population), which found that bulimics' risk of depression was 3.6 times higher in cases of associated anxiety disorders. Yet, that study did not take into account subjects' inpatient/outpatient status [20].

Thus, in the general population, and more so in the clinical population, the presence of anxiety disorders is associated with an increase in depression [34]. Subjects with depression and comorbid anxiety disorder more frequently seek treatment than subjects who are only depressed [35]. It is therefore not surprising that a frequent association is found between depression and anxiety disorders in subjects being treated for ED. The relationship between anxiety and depression is not specific to ED.

Although univariate analyses show that nearly all anxiety disorders are related to MDE, a separate analysis of each anxiety disorder reveals that they do not all have the same influence in terms of risk of onset of MDE in anorexics and bulimics, when adjusted for univariate variables related to MDE. Current generalized anxiety is significantly related to lifetime presence of MDE in AN subjects and to current MDE in AN and BN subjects. Generalized anxiety is the most frequent disorder in AN and BN subjects according to our study; it also appears to be one of the principal predictive factors for MDE, which is 2.4 to 4.2 times more frequent when GAD is present. It is interesting to note that in the general population, GAD is also the anxiety disorder most often associated with depression [34].

Diagnosis of OCD has its own particular effect on lifetime risk for MDE in AN subjects, regardless of GAD: it increases the risk of depression by 3.5. It is one of the most frequent anxiety disorders among AN subjects, present in nearly a quarter of them. This comorbidity is significantly higher than in bulimics and extremely high if it is compared with the frequency of OCD among psychiatric outpatients (9.2%) [36]. We have formulated the hypothesis that OCD may be one of the anxiety disorders that is predictive of an MDE specific to AN. This subject requires confirmation with further studies comparing the relationships between anxiety disorders and depression in AN subjects and subjects with MDE but not from AN.

Social phobia, one of the most frequent anxiety disorders in anorexics and bulimics, increases the current risk of MDE in anorexics by 3. However, the relationship between lifetime MDE and social phobia is far less significant than the association with OCD or generalized anxiety in AN and BN subjects. The significant comorbidity of social phobia with other anxiety disorders might partially explain this phenomenon. It has been shown, for example, that in the general population, generalized anxiety is associated with social phobia in 23% of the cases, and that this comorbidity is even higher in the clinical population [16]. Conversely, socially phobic subjects, in comparison with non–socially phobic subjects, display panic disorder from 3.24 to 10.6 times more often, OCD from 4.3 to 8.3 times more often, and agoraphobia from 2.56 to 2.83 times more often [37].

In bulimics, when GAD is excluded, two factors are related to current diagnosis of MDE: panic disorder and subjects' inpatient or outpatient status. Hospitalized bulimics are diagnosed with current MDE 4.2 times more often than those seen as outpatients. This corroborates a hypothesis, which has been retained in the literature for many years. Indeed very often, authors of studies on comorbidity in subjects with ED have postulated that hospitalized subjects presented more severe comorbid profiles than subjects treated as outpatients, but there has been no real demonstration of this assertion [22]. This result seems all the more significant in that it only concerns bulimics, yet this may be explained by the fact that ANs are more frequently hospitalized than BNs [38]. Indications for the hospitalization of AN subjects are most often based on the vital criteria of weight and less often on such psychic elements as suicidal risk or serious depression, both in France and in the United States [39,40]; conversely, in bulimics, hospitalization criteria often include these latter elements. Hospitalized bulimics are considered to be of a more serious nature in terms of comorbidity with depression. Despite this angle related to the usual hospitalization indications in bulimics, the presence of comorbidity with panic disorder and GAD remains associated with a current diagnosis of MDE. It has been shown that panic disorder, in the general population, is the cause of clinical situations that are serious and difficult to treat [15,41]; thus, we must be particularly attentive when taking on bulimic subjects who also display panic disorder and MDE.

We wish to determine the significance of the results regarding the onset of MDE and anxiety disorders. Indeed, the results we observed in subjects with ED are contrary to what has been observed in the general population, in which anxiety disorders usually emerge before depressive disorders [42]. For example, social phobia appears to precede depression in 95% of the cases in the general population [21]; yet in our AN and BN subjects, this was only true in 40% and 46.9% of the cases. The average age of onset of MDE is 16.2 years in anorexics and 17.0 in bulimics, and it is approximately 25 years in the general population (but can occur at any age). Does depression develop earlier in patients with ED, and is it more closely related to the EDs themselves than to anxiety disorders? This question merits exploration in further studies.

It would seem that ED is more closely associated with depression than with anxiety disorders if two things are taken into consideration: in a general population study, Zaider et al [43] showed that ED is significantly more frequent in teenagers manifesting a depressive or anxiety disorder than in those who manifest neither. More precisely, while controlling for the presence of anxiety disorder, having a depressive disorder was a significant predictor of ED; conversely, while controlling for the presence of depressive disorder, anxiety disorder predicted ED.

Further studies are necessary; they should be conducted using control groups of depressed subjects without ED to find out whether the results obtained here are specific to subjects with ED and, at the same time, to evaluate anxiety disorders, thymic disorders, and personality disorders in the general as well as the clinical population.

The results of this study should be considered with certain reservations. To begin with, we recruited patients seeking care in specialized ED centers, which do not represent all anorexic or bulimic subjects. The retrospective nature of the information collection may be a source of memorization bias, which might affect disorder diagnoses as well as their dates of onset and, therefore, their relative chronology of onset [44]. Furthermore, most patients

included in this study were adolescents or young adults, so it is important to note that all disorders that may develop after this inquiry have been unavoidably neglected. Finally, the diagnostic evaluation did not account for personality disorders (which, as we know, are frequently involved in requests for care) and the presence of depressive disorder in subjects with ED [38].

Depression in subjects with ED can be explained in part by comorbidity with OCD, generalized anxiety, social phobia, and panic disorder. Even if all anxiety disorders are frequent, and related to the possible presence of MDE, anorexic patients diagnosed with OCD or generalized anxiety are at a higher risk for depression than the others. Consequently, depression and anxiety should both be treated in subjects with ED; the presence of one increases the risk of the other, and their association is a significant, serious factor that can compromise patients' futures in that the anxiety-depressive comorbidity heightens social disability in comparison with subjects with anxiety only [45].

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