this report will heighten awareness to the fact that this syndrome can occur in nonambulatory patients.

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Comorbidity of Anxiety With Eating Disorders and OCD

TO THE EDITOR: The article by Walter H. Kaye, M.D., et al. (1) on comorbid anxiety disorders in eating disorders is a considerable contribution to this research area. However, other studies on this topic (2–4) were not referred to. Important information for several points of discussion is raised by these unmentioned studies.

We (2) found that 71% of 271 current subjects with eating disorders had lifetime comorbidity with at least one anxiety disorder (64% for Dr. Kaye et al.). The proportion of generalized anxiety disorder that was reported by Dr. Kaye et al. (10%) appears lower than our findings (anorexia nervosa: 45.6%, bulimia nervosa: 31.4%; all current). Converse to their finding, the eating disorders in our study group were all current, which may have affected the comorbidity rates. Given that subjects with a lifetime eating disorder (who are not currently ill) have a ratio of having no anxiety disorder to having an anxiety disorder significantly higher than for people who are currently ill (1), we wonder whether this discrepancy reflects a diagnostic bias instead of a bias of recall or a weak association with recovery. Indeed, high levels of anxiety and depressive symptoms (due to denutrition [5] or other factors, such as duration of illness, social disability, or preexisting trait anxiety) could lead to excessive current diagnoses of anxiety disorder.

Obsessive-compulsive disorders (OCDs) were nearly twice as frequent in the study of Dr. Kaye et al. (41%) as in our study (anorexia nervosa: 24.1%) and that of Iwasaki et al. (3). Although we did not use a symptomatic scale and thus may have missed some cases, the study by Iwasaki et al. suggests that it may rather be because the participants in the study by Dr. Kaye et al. "came from enriched pedigrees," leading to higher rates of comorbidity than in the community (1) or in other eating disorders groups.

Dr. Kaye et al. found that 66% of their comorbid cases and 42% of their entire study group had an onset of at least one anxiety disorder before the onset of an eating disorder. Our rates were, respectively, 50% and 33% (2). Although OCD and generalized anxiety disorder usually preceded the onset of an eating disorder in the study by Dr. Kaye et al., we observed the inverse pattern (2). This discrepancy could be due to some memory bias (i.e., people who have durably been characterized by obsessive-compulsive traits may have difficulties in remembering the exact time of the onset of OCD) or to a selection bias. Knowing that unusually precocious age at the onset of OCD is a risk factor for the development of eating disorders (6) and that the group selection of Dr. Kaye et al. was specific, we wonder whether the rate of early-onset OCD in their group of "enriched pedigrees" might have been unusually high.

Dr. Kaye et al. reported no differences in the rates of OCD between the patients with anorexia nervosa and those with bulimia nervosa, converse to another of their studies (4) in which they observed higher rates of OCD in patients with anorexia nervosa than in those with bulimia nervosa. In another of our studies (7), current diagnoses of agoraphobia and OCD were significantly more frequent in patients with anorexia nervosa than in those with bulimia nervosa. These contradictory results stress the need for developing further research on the comorbidity between eating disorders and anxiety disorders.

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TO THE EDITOR: We read with interest the report by Dr. Kaye et al. on the rates of comorbid anxiety disorders in individuals with eating disorders. The suggestion that child/adolescent-onset anxiety disorders may be associated with later eating disorders is particularly relevant to child mental health.

In women with eating disorders, the rates of OCD have been estimated at between 3% and 40%, according to diagnosis and group type. Some studies have also investigated the onset of OCD symptoms in women with eating disorders (1, 2).

Dr. Kaye et al. found an OCD lifetime prevalence of 41% in subjects with eating disorders; the onset of OCD was reported as preceding the eating disorders in 23% of the cases. The authors acknowledged that these rates were not comparable with rates found in community samples. They suggested that this might be because of the use of the Yale-Brown Obsessive Compulsive Scale as well as the Structured Clinical Interview for DSM-IV (SCID) to determine lifetime rates of OCD. Dr. Kaye et al. proposed that OCD cases could have been missed had the SCID been used on its own because the subjects did not recognize the nature of their symptoms and did not endorse the SCID screening probe for OCD. Dr. Kaye et al. did not comment on how the Yale-Brown Obsessive Compulsive Scale was used to diagnose OCD. The Yale-Brown Obsessive Compulsive Scale has been validated and is used to determine the severity of current OCD; its scoring is based on current impairment, distress, resistance to obsessions and compulsions, and time spent on these. It is not a diagnostic instrument (3), and to our knowledge, it has not been validated as a lifetime measure. We would be curious to see the rates of OCD diagnosed by this method in the comparison group.

If the average prevalence of eating disorders in females is 0.3% for anorexia nervosa and 1% for bulimia nervosa (4) and 23% (i.e., 0.3% of the females) had OCD before having an eating disorder, it would predict the development of an eating disorder in large numbers of girls with child/adolescent-onset OCD, or about 30%–100%. This would not be consistent with current clinical experience, although prospective studies of children with OCD are few. Dr. Kaye et al. acknowledged that their study group might have been biased because the subjects were recruited for a genetics study and were included if they had a relative with an eating disorder. We would like to highlight a caveat by Godart et al. (5) that "comorbidity studies have to be designed according to their specific goal, rather than being secondary results from other types of studies."

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TO THE EDITOR: Dr. Kaye et al. suggested that "childhood anxiety represents one important genetically mediated pathway toward the development of anorexia nervosa" (p. 2215) and that this is reflected in onset of OCD before anorexia. Dr. Kaye et al. reported that of 94 patients with anorexia nervosa, 35% also had OCD. Upon examination of these, about 12% dropped out, and of those remaining, 23% had OCD before they had anorexia nervosa. Thus, 94×35%×88%×23%= seven individuals of 94 (7%) had OCD before they had anorexia nervosa. A French study on the same topic (1) reported that two (7%) of 29 patients had OCD before they had anorexia nervosa. Thus, the expression of OCD before anorexia nervosa is rare.

The lifetime prevalence of anxiety disorders has been reported to be very high, with estimates as high as 12%–18% and even 30% (see Dr. Kaye et al.) having been reported. Because the incidence of OCD increases exponentially when an individual approaches puberty and there are no sex differences in OCD (2), we must conclude that the major expression of the "genetically mediated pathway" for anxiety disorders that Dr. Kaye et al. suggested is a "pathway toward the development of anorexia nervosa" occurring much later than the onset of anorexia nervosa. Also, we must assume that these hypothetical genes are expressed as anorexia only in girls (the prevalence of anorexia is very low in boys) but that the same genes are expressed as OCD in both girls and boys. Whether genes with such time-dependent, sexually dimorphic phenotypic expression patterns exist remains to be investigated.

Furthermore, although it is apparently possible to diagnose OCD retrospectively at 5 years (see Kaye et al.) or even at 3 years of age (1), it appears that childhood OCD is 8–12 times more prevalent in the United States (see Dr. Kaye et al.) than in England (2). If OCD causes anorexia, one would expect anorexia nervosa to be about 10 times more prevalent in the United States than in England. There is no evidence that this is the case. The available evidence does not support the hypothesis that OCD is a risk factor for the development of anorexia nervosa.

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Dr. Kaye and Colleagues Reply

TO THE EDITOR: We appreciate the interest and comments of Dr. Godart et al., Drs. Micali and Heyman, and Drs. Södersten and Bergh. We regret that space limitations preclude a comprehensive review of all literature relating to anxiety and eating disorders. Nonetheless, we note that there are more similarities than differences between our results and those of Dr. Godart et al. once we account for differences in sampling and possible cultural differences.

There are some notable differences in the types of anxiety disorders diagnosed between our two studies, although the

overall prevalence of anxiety disorders was similar. The most notable differences rest with the observed prevalence of OCD in our group and the absence of significant differences in the prevalence of OCD between participants with anorexia and patients with bulimia nervosa—both of which surprised us as well. It is important to note that our study group was collected from nine different sites in North America and Europe and thus was unlikely to reflect a single-site bias. In an earlier study (1), we found that the form of OCD most commonly observed in individuals with eating disorders is characterized by a focus on symmetry, exactness, and order. It is likely that researchers who do not routinely assess this variant of OCD may detect fewer cases of OCD. We acknowledge that particular factors may have enriched our study group for certain traits. For example, it is possible that families with more obsessional traits may have been more successful in completing the extensive diagnostic and blood collection protocols of our genetic study or that certain disorders may have been more common in families that have two or more members with an eating disorder. Regardless, both our study and that of Dr. Godart et al. highlight that there is a strong relationship between eating disorders and anxiety disorders, although much remains to be learned about shared phenomenology or biology.

In answer to Drs. Micali and Heyman, the diagnosis of OCD was made with the Structured Clinical Interview for DSM-IV (SCID), not with the Yale-Brown Obsessive Compulsive Scale. The latter was used to identify specific obsessions and compulsions and to rate the severity of the disorder. We stipulated that by using the Yale-Brown Obsessive Compulsive Scale first, we were likely to identify more cases by reminding subjects of symptoms, such as symmetry/exactness, which might be overlooked in response to a general screen, such as the SCID's. The method of ascertainment of OCD in the comparison subjects was different so that a direct comparison is not possible. However, an earlier study that used similar methods (reference 4 of the letter of Dr. Godart et al.) found two women with OCD in a group of 44 women in the community.

The SCID assesses current (in the past 6 months) generalized anxiety disorder only. Furthermore, the screen asks whether subjects have been "particularly nervous or anxious" in the past 6 months. People who are always nervous or anxious often deny being "particularly" anxious in the past 6 months (there is no difference from their usual elevated state of anxiety). Thus the SCID may miss the diagnosis in subjects having the disorder whose current level of anxiety is not higher than their usual level. That is a shortcoming of the instrument. Furthermore, our study group contained many recovered subjects, whereas the group of Dr. Godart et al. consisted of those with current eating disorders. Because anxiety may be elevated in those who are currently ill with eating disorders, this could account for a significant amount of the discrepancy.

Observed comorbidity in a group can reflect several underlying processes:

1. Two disorders can share the same underlying continuum of liability.
2. The affection status of one disorder can increase the risk for the second.
3. Extreme cases of one disorder only can increase the risk for the second disorder.
4. Three independent disorders can exist in which excess comorbid cases are due to a separate third disorder.
5. Risk factors for the two disorders correlate.
6. The liability for one disorder is a cause of the other disorder (2).

Our study group was not appropriate to tease out the underlying cause of comorbidity in eating and anxiety disorders, nor did we claim to do so. In our genetic study, we were less interested in addressing the underlying process of comorbidity that can be addressed more effectively in population-based samples, and more interested in identifying patterns of comorbidity in families enriched for anorexia nervosa that may assist us with the refinement of phenotypes for genetic studies.

As for the comments of Drs. Södersten and Bergh, our article did not break down by subgroups the rates of childhood onset of OCD before the onset of eating disorders. Our calculations show that when the entire group of subjects with anorexia nervosa is taken into consideration, at least 14% of the subjects with anorexia nervosa had an onset of OCD before they developed anorexia nervosa. In comparison, 24% of the subjects with anorexia nervosa and bulimia nervosa and 22% of those with bulimia nervosa had an onset of OCD before they developed an eating disorder when the entire study group is studied. We should have noted in the article that the focus of the study was on relative pairs affected by bulimia nervosa and that the anorexia nervosa group was relatively small and might have been skewed because of how the subjects were selected. In a more recent study (unpublished data), we collected 744 subjects with anorexia nervosa and bulimia nervosa in which the entry criterion was a diagnosis of anorexia nervosa. Fifty-seven percent of the entire anorexia nervosa/anorexia nervosa and bulimia nervosa group had a lifetime diagnosis of OCD, and 36% of the entire group had an onset of OCD before the onset of anorexia nervosa or anorexia nervosa and bulimia nervosa. These data support our contention that a premorbid onset of OCD is common in people who later develop anorexia nervosa.

The point of this article was to identify susceptibility factors that may precede the onset of anorexia nervosa. As noted in our article, other recent studies clearly show that anxious, obsessional, and perfectionistic traits commonly occur in childhood and predate the onset of anorexia nervosa. It is also important to recognize that obsessional traits that are known to be common in anorexia nervosa might be described as OCD, obsessive-compulsive personality disorder, a rigid perfectionistic temperament, or other diagnoses depending on the assessment instrument and perhaps the bias of the investigator. It is well recognized by experts in the field of behavior that a DSM diagnosis, while a necessary attempt to categorize illness, may not necessarily reflect how behavior is coded in the brain. We need to continue to better characterize these traits and understand their pathophysiology rather than get caught up in unanswerable arguments about whether anorexia nervosa is a variant of another DSM diagnostic category.

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Suicide Risk in Placebo-Controlled Trials of Bipolar Disorder

TO THE EDITOR: Jitschak G. Storosum, M.D., Ph.D., and colleagues (1) addressed the important issue of placebo-controlled trials of bipolar disorder and noted that there are ethical problems in using placebo when effective treatments are available, particularly when there is a risk of suicidal behavior. They noted in the abstract that concern about the risk of suicidal behavior "should not be an argument against the conduct of placebo-controlled trials for these indications, provided that appropriate precautions are taken" (p. 799). However, is such a conclusion scientifically credible, logical, or, indeed, ethical when seven of 11 studies examining the treatment of manic episodes and all four studies of the prevention of manic/depressive episodes excluded suicidal patients? Perhaps "appropriate precautions" implies not including those who are suicidal, which—contrary to the assertion in the authors' conclusion—seems to indicate that there is concern about the risk of suicidal behavior in such placebo-controlled trials.

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Dr. Storosum and Colleagues Reply

TO THE EDITOR: We agree with Dr. Goldney that in bipolar disorder there is an increased risk of suicidal behavior (1). We investigated only whether there is a greater risk of suicide in the placebo arms of placebo-controlled studies than in the active arms, and we found no difference between the two conditions.

Dr. Goldney would like us to clarify the meaning of "appropriate precautions" and asks whether this implies the exclusion of those who are suicidal. Indeed, in most studies, suicidal patients are explicitly excluded. However, this is not the meaning of "appropriate precautions." By "appropriate precautions," we mean the usual precautions that are taken before and/or during the studies (the inclusion and exclusion criteria, careful monitoring, etc.). When these appropriate precautions are taken, we have shown that concern about the risk of suicidal behavior is not an argument against the conduct of placebo-controlled trials for these indications. This conclusion is evidenced based and therefore credible, logical, and, indeed, ethical.

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New Mnemonic for Depressive Symptoms

TO THE EDITOR: We wish to communicate a critical concern pertaining to psychiatric training and to the practice of psychiatry. Within the United States, there is a widely accepted standard mnemonic device that is proposed to aid clinicians in recalling and assessing the presence of the symptoms of a major depressive episode as enumerated in DSM-IV. This alphabetic mnemonic, "SIGECAPS," is presumably often promulgated in the teaching/training curricula of psychiatry and other disciplines (1).

With the increasing and appropriate recognition of the ubiquity of major depression in general and clinical populations (2), we might extrapolate that the mnemonic SIGECAPS pervades the knowledge base accepted among professionals within the vast fields of medicine, psychology, and social science (3). SIGECAPS stands for **S**leep disturbance, **I**nterest (diminished), **G**uilt or feeling worthless, **E**nergy (loss), **C**oncentration difficulties or indecisiveness, **A**ppetite abnormality or weight change, **P**sychomotor retardation or agitation, and **S**uicide or death (acts or thoughts of).

The relevance of identifying and monitoring the progression of the symptoms of major depression is scientifically sound and nearly universally granted among mental health practitioners. As such, it will not require elaboration here.

The mnemonic SIGECAPS, although phenomenologically accurate and routinely applied, is not without significant shortcomings. It is our opinion that phonologically, heuristically, and aesthetically, this acronym is less than ideal for meaningful assimilation and practical application by students and practitioners within the multifarious disciplines pertaining to human behavior. Furthermore, the repetition of the letter "S" in the acronym, to represent both sleep disturbance and suicidal ideation, would appear to diminish the ease of remembering which symptom the "S" is intended to stand for in each instance.

We propose an alternative mnemonic: "C GASP DIE." While it is equally accurate and at least as practical, we believe it to be superior to the conventional SIGECAPS in its connotations of the morbidity/mortality of major depression, its resultant ease of recollection, and its subjective aesthetic appeal. C GASP DIE stands for **C**oncentration difficulties or indecisiveness, **G**uilt or feeling worthless, **A**ppetite abnormality or weight change, **S**leep disturbance, **P**sychomotor retardation or agitation, **D**eath or suicide (thoughts or acts of), **I**nterest (diminished), and **E**nergy (loss).

It is our hope that educators and opinion leaders within the fields we mention will consider adopting the new acronym, "C GASP DIE," for its speculatively superior qualities pertain-