The Empirical Basis of Generalized Anxiety Disorder

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Objective: The authors review the empirical data on generalized anxiety disorder, a diagnostic category that has been among the more conceptually challenging in psychiatric nosology. Method: Published studies and recent findings that were considered by the Generalized Anxiety Disorder Subcommittees of the DSM-IV Anxiety Disorders Work Group are reviewed. Among the issues examined are diagnostic reliability, comorbidity, boundaries with other disorders, and clinical features. Results: A variety of data on the reliability and validity of generalized anxiety disorder have been produced. Some authors have suggested that generalized anxiety disorder is better conceptualized as a vulnerability that should be located on axis II, and others have recommended that the category be eliminated. Although the diagnostic reliability of generalized anxiety disorder is lower than that of other anxiety disorders, the features constituting the diagnostic criteria for generalized anxiety disorder have been found to be reliable. An important development has been the determination of a set of somatic symptoms associated with generalized anxiety disorder that differs substantially from those for other anxiety disorders. These findings led to reduction in the number of items in the symptom criteria, from 18 in DSM-III-R to six in DSM-IV. Another substantial revision is greater emphasis on the uncontrollability of worry. Conclusions: Whereas the data on construct and discriminant validity, age at onset, course, familial transmission, and response to treatment generally support the DSM-IV definition of generalized anxiety disorder, the construct continues to have weaknesses and further research is needed. (Am J Psychiatry 1994; 151:1272–1280)

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In the 7 years since generalized anxiety disorder was reformulated, numerous studies have produced data bearing on the reliability and validity of the disorder and its defining features. The purpose of the present paper is to review the collective findings on the reliability and validity of generalized anxiety disorder and the role these data played in the deliberations of the Generalized Anxiety Disorder Subcommittee of the DSM-IV Anxiety Disorders Work Group. Among the issues to

be considered are diagnostic reliability (e.g., interrater agreement), rates and patterns of comorbidity, boundary issues such as distinguishability from “neighboring” disorders (e.g., obsessive-compulsive disorder), and other clinical features (e.g., type of onset, age at onset, familial/genetic data, treatment response). In addition, the reliability and validity of specific features constituting the diagnostic criteria for generalized anxiety disorder (i.e., excessive worry, associated symptoms) will be discussed.

Validity at the Syndrome Level

Studies examining the reliability of the DSM-III-R anxiety disorders have shown consistently that generalized anxiety disorder is among the disorders with the lowest diagnostic agreement (4, 5). For example, in a recent study from our clinic (4), the kappa for generalized anxiety disorder as a principal diagnosis was 0.57. Moreover, investigators examining rates and patterns of comorbidity have noted that generalized anxiety disorder is the most frequently assigned additional diagnosis in patients with a principal anxiety or mood disorder (6–8). In addition, when generalized anxiety disorder is the principal diagnosis, it is associated with the highest rates of comorbidity among the DSM-III-R anxiety disorders (6, 7, 9). With regard to classification, these findings might be interpreted as reflecting poor discriminant validity among generalized anxiety disorder and other diagnostic categories—namely, as indicating that the diagnostic system is distinguishing phenomena (i.e., features of generalized anxiety disorder) that could be categorized more parsimoniously if combined. Perhaps it is this issue that poses the most substantial threat to the validity of generalized anxiety disorder. Indeed, this disorder was the focus of considerable debate during the evaluation and revision of the criteria for DSM-IV. For these and other reasons, some involved in the DSM-IV process suggested that the evidence might not be sufficiently strong to retain generalized anxiety disorder as a diagnostic category and that it might be better placed in the appendix of disorders in need of further study.

Factors Relating to Diagnostic Reliability

Given the salience of diagnostic reliability for the issue of the syndrome validity (6), it is important to consider factors that may be contributing to the lower rates of diagnostic agreement for DSM-III-R generalized anxiety disorder. For example, recent conceptualizations of generalized anxiety disorder have referred to the diagnosis as the “basic” anxiety disorder because its defining features (i.e., worry or “anxious expectation,” hyperarousal) reflect basic processes of anxiety (1, 10). If this is indeed the case, then one would expect that the distinctiveness of generalized anxiety disorder would be mitigated by the fact that its features are present to some extent in all of the DSM-III-R anxiety disorders, and possibly the mood disorders as well. Thus, whereas

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Another factor that has been posited to contribute to the lower diagnostic reliability of generalized anxiety disorder is the fact that the diagnosis lacks a clear behavioral marker to facilitate its differentiation (e.g., compulsions in obsessive-compulsive disorder). Indeed, the existing diagnostic reliability data (4) indicate that diagnoses with these features (e.g., simple phobia, obsessive-compulsive disorder) evidence higher rates of agreement than those without overt markers (e.g., generalized anxiety disorder, panic disorder without agoraphobia).

In another study producing data bearing on this issue, Zinbarg and Barlow (unpublished 1994 manuscript) examined the construct validity of the anxiety disorders by means of the factor analysis of scores from 23 subscales of measures included in an initial intake battery assessing anxiety and related dimensions (e.g., panic, anxiety sensitivity, depression, compulsions, social anxiety). The subjects were 432 patients consecutively admitted to an outpatient anxiety disorders clinic and 32 normal comparison subjects. Five primary factors (panic, agoraphobia, social anxiety, compulsions, general anxiety) and a higher-order factor (negative affect) were derived. Using factor scores calculated for each subject, the authors examined the extent to which the different DSM-III-R anxiety disorder diagnoses evidenced characteristic factor-score profiles through discriminant analysis. Whereas certain diagnostic groups had significantly higher scores on a specific factor (e.g., the patients with social phobia had significantly higher scores on social anxiety than the other groups), the patients with generalized anxiety disorder, although having higher scores than the normal comparison subjects on all factors, were not differentiated from the other anxiety disorder groups on any one factor. Nevertheless, profile analyses revealed significant differentiation between the patients with generalized anxiety disorder and the other groups, indicating that the patients with generalized anxiety disorder had a characteristic factor-score profile. Consistent with the position we have outlined, these results indicate that, whereas the patients with generalized anxiety disorder could not be differentiated on the basis of any one specific dimension assessed in this study (thus attesting to a proposed source of lower diagnostic reliability), their presentation was unique with regard to their profile of scores on a variety of dimensions of anxiety. Moreover, it is possible that there are other specific dimensions (not tapped by the measures used in the study) that would differentiate patients with generalized anxiety disorder from other groups.
GENERALIZED ANXIETY DISORDER

It does not appear that the lower diagnostic reliability of generalized anxiety disorder is due to a problem in the boundary with obsessive-compulsive disorder. This is noteworthy because the features of obsessive-compulsive disorder may be conceived as having the most overlap with features of generalized anxiety disorder (e.g., pervasive worry versus obsessions, characterological presentation). Evidence for the distinguishability of generalized anxiety disorder and obsessive-compulsive disorder was obtained by Brown et al. (11), who contrasted 46 patients with generalized anxiety disorder and 31 patients with obsessive-compulsive disorder on the basis of data obtained through interviews with the Anxiety Disorders Interview Schedule—Revised (12) and questionnaires. Of the 55% of the subjects who received two independent interviews, in no case did one interviewer assign a principal diagnosis of obsessive-compulsive disorder and the other assign a diagnosis of generalized anxiety disorder, which strongly suggests that choosing between these two diagnoses was not a difficult differential diagnostic decision. Moreover, examination of comorbidity patterns indicated that generalized anxiety disorder and obsessive-compulsive disorder rarely co-occurred (patients with obsessive-compulsive disorder plus generalized anxiety disorder, 7%; patients with generalized anxiety disorder with additional obsessive-compulsive disorder, 2%).

Familial Transmission

Data from family and twin studies have provided mixed support for the validity of generalized anxiety disorder; some studies show a familial aggregation (15, 16, 25), and others have not (21, 26). However, interpretation of these collective findings is difficult because of the substantial differences in methods (e.g., blindness of interviewers, interview type, subject selection) and definitions of the disorder (e.g., "anxiety neurosis," DSM-III, DSM-III-R) among studies.

Findings from two studies indicate that DSM-III generalized anxiety disorder is discriminable from panic disorder on the basis of the familial aggregation of the two disorders (15, 16). In the Noyes et al. study (15), the findings revealed a higher frequency of generalized anxiety disorder among first-order relatives of probands with generalized anxiety disorder than among relatives of nonanxious comparison probands and probands with panic disorder or panic disorder with agoraphobia. In addition, the high frequency of panic disorder and panic disorder with agoraphobia among the relatives of probands with panic disorder or panic disorder with agoraphobia, respectively, was not observed in the families of the probands with generalized anxiety disorder, indicating specificity in the patterns of these aggregations. These data should be interpreted cautiously since the diagnoses were not established blindly and the numbers of subjects were small (e.g., 20 probands with generalized anxiety disorder). Nonetheless, in a more recent study, Noyes et al. (16) replicated these familial aggregation data when using larger groups of subjects with generalized anxiety disorder (N=41) and panic disorder (N=71) who had been diagnosed by means of the DSM-III-R criteria and the Structured Clinical Interview for DSM-III-R (27).

The authors of a recently published study of 1,033 blindly assessed female-female twin pairs from a population-based registry concluded that generalized anxiety disorder is a 'moderately familial disorder, with heritability calculated to be around 30% (25). However, the results were somewhat counter to prediction in that the evidence for heritability was stronger and more consistent when generalized anxiety disorder was diagnosed by using a 1-month duration than when a 6-month duration criterion. For using 1-month duration criterion, the results clearly suggested that the heritability of generalized anxiety disorder was not due to comorbidity with major depression or panic disorder. By using the 6-month duration criterion, the results were considerably less clear, probably because of the small numbers of affected twins. These findings were tempered further by the fact that the authors used an older version of a structured interview. Consequently, although the diagnosis of generalized anxiety disorder was based largely on DSM-III-R criteria, the requirement that "worry" affected two or more life circumstances was not assessed (25, p. 263). Two previous twin studies examining DSM-III generalized anxiety disorder failed to demonstrate conclusively the role of genetic factors in generalized anxiety disorder (26, 28).

Comorbidity and Other Boundary Issues

One of the primary concerns raised about the validity of the diagnosis of generalized anxiety disorder is the fact that it is associated with high rates of comorbidity, as both a principal diagnosis and an additional diagnosis. For instance, Brown and Barlow (6) found that 82% of patients with a principal diagnosis of generalized anxiety disorder had at least one additional diagnosis. This high rate of comorbidity is another factor that lowers the diagnostic reliability of generalized anxiety disorder; pure generalized anxiety disorder seems to be relatively rare. Consequently, diagnosticians must frequently determine whether patients' presenting symptoms warrant a separate diagnosis of generalized anxiety disorder, as opposed to being associated symptoms of the co-occurring conditions.

Accordingly, some researchers involved in the DSM-IV process have interpreted the comorbidity findings to indicate that, diagnostically, it would be more parsimonious to subsume generalized anxiety disorder under the conditions with which it co-occurs. However, this position may be flawed in a number of ways. On a practical note, adopting this position would result in the loss of coverage in the diagnostic system of a substantial number of patients who are assigned generalized anxiety disorder without any additional diagnoses (approximately 20%-26% in some clinics). Moreover, it is a consistent finding in cross-sectional comorbidity studies that roughly 50% of patients with a principal anxiety disorder have at least one additional diagnosis; many principal diagnoses, in addition to generalized anxiety disorder, have comorbidity rates well above this figure (e.g., 73% of patients with a principal DSM-III-R diagnosis of panic disorder with severe agoraphobia are assigned at least one additional diagnosis) (6). Thus, high comorbidity rates among the DSM-III-R anxiety disorders are not unique to the diagnosis of generalized anxiety disorder.

It is interesting that the clinical features of several of the diagnoses that most frequently co-occur with generalized anxiety disorder ostensibly possess little overlap with the features of generalized anxiety disorder. For example, in the studies by Brown and Barlow (6) and others (7), the most commonly occurring additional diagnosis in patients with generalized anxiety disorder was social phobia (29% and 23%, respectively), a diagnosis infrequently involving chronic anxiety and worry except in the cases of patients with severe generalized social phobia. In the study
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With regard to the mood disorders, Brown and Barlow (6) noted that 18% and 11% of patients with generalized anxiety disorder had an additional diagnosis of dysthymia and major depression, respectively. Thus, the majority (71%) of patients with generalized anxiety disorder in this study had symptoms that could not be subsumed under an affective disorder. In addition, Noyes et al. (16) noted that major depression co-occurred significantly less frequently in patients with generalized anxiety disorder than in patients with panic disorder. However, these observations are tempered by the findings from two recent studies that yielded higher rates of comorbid major depression and generalized anxiety disorder: 46% in a study by Masson et al. (9) and 34% in a study by Noyes et al. (16). Moreover, it should be noted that the rates of comorbid generalized anxiety disorder, major depression, and dysthymia were calculated on the basis of DSM-III-R criteria, which state that generalized anxiety disorder should not be diagnosed if the disturbance occurs “only during the course of a Mood Disorder.” Thus, the possibility exists that the comorbidity rates for generalized anxiety disorder and the mood disorders would be much higher if this diagnostic hierarchy rule had been omitted in these studies.

Another difficulty with the position that generalized anxiety disorder could be subsumed under other diagnoses is the fact that this argument discounts findings pertaining to temporal sequence and the fact that generalized anxiety disorder often has an earlier onset than many of the disorders with which it frequently co-occurs (e.g., panic disorder). Accordingly, findings of high comorbidity could be interpreted in a fashion noted earlier, as meaning that the features of generalized anxiety disorder may increase vulnerability to the subsequent development of these co-occurring conditions. Further research examining the longitudinal course and/or lifetime prevalence of disorders is needed to corroborate this assertion.

Another important issue is the clarification of the boundary between generalized anxiety disorder and the patients' clinical symptoms of anxiety and depression that seem to be severe enough to warrant a diagnosis but do not reach the threshold for generalized anxiety disorder for various reasons (e.g., lower severity ratings, insufficient number of symptoms, presence of somatic symptoms without excessive worry). Whereas initial observations indicated that these subthreshold
cases are prevalent in primary care settings, until recently it was speculated that a substantial proportion of these cases might meet the diagnostic threshold for established diagnoses, such as generalized anxiety disorder and dysthymia, under conditions of more rigorous, structured evaluation. Accordingly, as part of the DSM-IV process, a field trial examined the presenting symptoms in these patients (29). In addition to determining whether these cases were indeed subthreshold on the basis of structured interviewing, the field trial addressed such issues as the prevalence of this presentation and the extent to which depressive symptoms occurred.

Results from that study (29) indicated that cases with affective symptoms that are subthreshold with respect to DSM-III-R anxiety or depressive disorders but present substantial functional impairment or distress do appear to exist and are relatively common. However, close examination indicates that these cases differ in a number of important ways from those meeting the criteria for DSM-III-R generalized anxiety disorder or a DSM-III-R mood disorder. Basically, patients with these conditions had neither the pure depressive symptoms nor the pure anxiety symptoms that form the core of one of the other major set of disorders (based on factor analyses). Profile analyses comparing these patients with patients who had anxiety or mood disorders also revealed significant differences on the major factors of anxiety, depression, negative affect, and physiological symptoms. Because these patients had very heterogeneous presentations, with symptoms comprising the superordinate factor of negative affect without a predominance or clear pattern of pure anxiety or depressive symptoms, the most satisfactory solution would be not to force their conditions into either anxiety or mood disorders but, rather, to identify them, in a preliminary way, as a separate category of “mixed anxiety-depression.”

Response to Treatment

Although there are inherent difficulties in attempting to validate a diagnostic entity on the basis of its response to treatment, it is interesting that patients with generalized anxiety disorder have tended to respond less favorably to conventional cognitive-behavioral treatments than to patients with other anxiety disorders, such as panic disorder (30, 31). In the majority of outcome studies conducted thus far, the treatments examined have been relatively nonspecific (e.g., relaxation training, cognitive restructuring); that is, unlike treatments for other anxiety disorders that have been found to be highly effective (e.g., treatments for panic disorder, social phobia, obsessive-compulsive disorder), the treatments examined in many of these studies have not contained components tailored to address disorder-specific key features (e.g., excessive worry). Although a lower level of diagnostic reliability may certainly be a contributory factor, perhaps it is partly because of the lower degree of treatment specificity that few comparative outcome studies of generalized anxiety disorder have shown differences in the effectiveness of active treatment conditions (32). However, more recent evidence from single-case studies, although preliminary, indicates that newly developed interventions designed specifically to target the worry associated with generalized anxiety disorder may be effective in the treatment of generalized anxiety disorder (33, 34). An important issue awaiting further research is whether highly specialized treatments produce gains over the modest improvements achieved by the less specific treatments that have been evaluated to date.

A large number of studies suggest that pharmacological treatments, particularly the benzodiazepines, are effective for generalized anxiety disorder, although these results are typically relatively weak and short-lived (35). Nevertheless, as many as 40% of patients achieve a remission of symptoms. More recently, however, reports have indicated a lack of differences between drug and placebo in studies examining the pharmacological treatment of generalized anxiety disorder. This is an interesting and important issue that deserves further consideration. Swinson et al. (36) reviewed 39 studies involving pharmacological treatment of generalized anxiety disorder. The most frequently investigated drugs were buspirone (41%) and diazepam (36%). The most common assessment measure was the Hamilton Anxiety Rating Scale. Structured interviews were used in only 20% of the studies; the reports on the majority of studies referred only to some type of unspecified “clinical interview.” Swinson et al. concluded that, given the difficulty in diagnosing generalized anxiety disorder, many of the studies that did not use structured interviews might have included a heterogeneous mix of patients with vague symptoms of anxiety and depression. Hence, the authors strongly recommended careful assessment of these patients with structured interviews to clearly identify generalized anxiety disorder.

In addition, recent reports indicate that differences between drug and placebo for generalized anxiety disorder seem to be easier to find in primary care settings (L.D. Bradford, personal communication, 1992; K. Rickels, personal communication, 1992). Lower rates of response to placebo are also found in these settings. The reasons for these discrepancies are not clear. In summary, clarification of treatment response issues awaits future investigation that uses more precise methods and clearer identification of patients.

RELIABILITY AND VALIDITY OF DIAGNOSTIC FEATURES

Despite the fact that the diagnostic reliability of generalized anxiety disorder is lower than that of other anxiety disorders, the features constituting the diagnostic criteria for generalized anxiety disorder have been found to be reliable. For instance, several studies have shown that the content and presence of the spheres of worry involved in generalized anxiety disorder can be identified reliably (18, 37-39). Findings from initial studies have indicated that, whereas ratings of the individual symptoms constituting the associated symptom criterion for generalized anxiety disorder are unreliable (37, 40), algorithms involving symptom areas or groups of symptoms (e.g., interrater agreement on the identification of six or more symptoms) can evidence good reliability (P.A. DiNardo, unpublished 1991 manuscript).

Nevertheless, a recently completed study indicated that the majority of the individual symptom ratings can be established reliably. In this study (41), the interrater reliability and endorsement rates for the 18 associated symptoms were calculated from interview-based ratings of 204 patients with generalized anxiety disorder at four sites. The data on interrater reliability indicated that 16 of the 18 symptoms evidenced agreement at a level greater than chance (dizziness and trembling were the exceptions). Despite the use of different sites and interviews, significant Spearman correlations ranging from 0.69 to 0.94 revealed marked consistency in the rates of symptom endorsement across sites. Interestingly, the most reliable and most frequently endorsed symptoms corresponded to all of those listed in the vigilance and scanning cluster and most of the symptoms of the motor tension cluster of DSM-III-R; none of the autonomic hyperactivity symptoms met these reliability and endorsement criteria.

Although these data indicate that the spheres of worry associated with generalized anxiety disorder and the majority of the associated symptom ratings can be established reliably, the ability of these features to differentiate patients with generalized anxiety disorder from other patient and nonpatient groups must be considered as well. Studies examining the nature of worry in patients with generalized anxiety disorder and nonanxious comparison subjects (38, 39) have produced findings indicating that, although these groups do not differ substantially in the content of their worries, there are considerable differences in measures reflecting controllable and pervasive anxiety. The worry process (e.g., percentage of the day involved in worrying, frequency of unprecipitated worry, self-perceptions of controllability and realism of worry, number of worry topics). In addition, whereas 100% of patients with generalized anxiety disorder in a recent study (T.D. Borkovec, unpublished 1992 manuscripts) reported experiencing their worry as uncontrollable and interfering with attention, few nonanxious comparison subjects reported these measures of worry (0% and 15%, respectively).

Although the data are limited, particularly with regard to between-group comparisons of controllability of the worry process, indexes of this nature appear to differentiate patients with generalized anxiety disorder from other anxiety disorder groups. For example, Sanderson and Barlow (18) found that a greater proportion of patients with generalized anxiety disorder than patients with other anxiety disorders (social phobia, panic disorder, simple phobia, obsessive-compulsive disor-
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Note that differences in generalized anxiety disorder may have been replicated in a study comparing patients with generalized anxiety disorder to patients with obsessive-compulsive disorder (11). Moreover, in at least three studies (11, 42, 43), patients with generalized anxiety disorder had significantly higher scores than other anxiety disorder groups (including patients with obsessive-compulsive disorder) and normal comparison subjects on the newly developed Penn State Worry Questionnaire, a psychometrically validated measure of the trait of worry.

Data concerning the discriminant validity of the 18 symptoms constituting the associated symptom criterion of generalized anxiety disorder in DSM-III-R are relatively sparse. The few studies addressing this issue have produced converging evidence of the low rate of endorsement of autonomic symptoms by patients with generalized anxiety disorder on diagnostic interviews (13, 16, 41). In fact, a potential discriminating feature of generalized anxiety disorder is the observation that patients with generalized anxiety disorder respond to psychological stress with autonomic inaccessibility; that is, relative to nonanxious comparison subjects, patients with generalized anxiety disorder show less variability in autonomic responses (e.g., heart rate, skin conductance) to laboratory-based psychological challenges (44-46).

The one laboratory-based measure that has been found (45) to differentiate patients with generalized anxiety disorder can be identified reliably (18, 37-39). Findings from initial studies have indicated that, whereas ratings of the individual symptoms constituting the associated symptom criterion for generalized anxiety disorder are unreliable (37, 40), algorithms involving symptom areas or groups of symptoms (e.g., interrater agreement on the identification of six or more symptoms) can evidence good reliability (F.A. DiNardo, unpublished 1991 manuscript).

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Although these data indicate that the spheres of worry associated with generalized anxiety disorder and the majority of the associated symptom ratings can be established reliably, the ability of these features to differentiate patients with generalized anxiety disorder from other patient and nonpatient groups must be considered as well. Studies examining the nature of worry in patients with generalized anxiety disorder and nonanxious comparison subjects (38, 39) have produced findings indicating that, although these groups do not differ substantially in the content of their worries, there are considerable differences in measures reflecting controllability and pervasiveness of the worry process (e.g., percentage of the day involved in worrying, frequency of unprecipitated worry, self-perceptions of controllability and realism of worry, number of worry topics). In addition, whereas 100% of patients with generalized anxiety disorder in a recent study (T.D. Borkovec, unpublished 1992 manuscript) reported experiencing their worry as uncontrollable and interfering with attention; few nonanxious comparison subjects reported these measures of worry (0% and 15%, respectively).

Although the data are limited, particularly with regard to between-group comparisons of controllability of the worry process, indexes of this nature appear to differentiate patients with generalized anxiety disorder from other anxiety disorder groups. For example, Sanderson and Barlow (18) found that a greater proportion of patients with generalized anxiety disorder than patients with other anxiety disorders (social phobia, panic disorder, simple phobia, obsessive-compulsive disorder) reported worrying excessively over minor matters. In a similar analysis, DiNardo (unpublished 1991 manuscript) examined the discriminatory power of the item “Do you worry excessively about minor matters?” from the Anxiety Disorders Interview Schedule—Revised by comparing the frequencies of affirmative responses to this question by patients with generalized anxiety disorder and patients with other anxiety disorders. The positive predictive power of this question was 0.36 (the probability of a generalized anxiety disorder diagnosis, given an affirmative response); the negative predictive power was 0.94 (the probability of not having a generalized anxiety disorder diagnosis, given a negative response). These findings indicate that, although an affirmative response to the question about excessive worry over minor matters cannot confirm a diagnosis of generalized anxiety disorder, a negative response can rule out generalized anxiety disorder with confidence. Recent supporting evidence was provided by the unpublished study by Borkovec, who found that patients with generalized anxiety disorder could be differentiated from other anxiety disorder groups by the “Do you worry excessively about minor matters?” item from the Anxiety Disorders Interview Schedule—Revised (generalized anxiety disorder, 93%; other anxiety disorders, 32%-71%). Moreover, Borkovec found that patients with generalized anxiety disorder experienced a significantly greater degree of life interference associated with their worry than did patients with other anxiety disorders.
anxiety disorder from nonanxious comparison subjects at baseline and in response to psychological challenge is muscle tension (i.e., increased frontalis and gastrocneumius electromyogram activity). Indeed, this finding parallels recent data obtained through self-report measures (questionnaires, interviews) indicating that symptoms of motor and psychic tension (e.g., muscle tension, irritability, feeling keyed up or on edge) are the most frequently reported by patients with generalized anxiety disorder (41). In fact, preliminary evidence attesting to the discriminant validity of these symptoms was the finding by Brown et al. (42) that patients with generalized anxiety disorder were differentiated from all other DSM-III-R anxiety disorder groups except patients with obsessive-compulsive disorder on the basis of their scores on the tension subscale of the Self-Analysis Questionnaire, a measure of current (past week) symptoms. Examination of the tension subscale reveals that many of the items correspond to symptoms from the vigilance and scanning cluster and the motor tension cluster of the DSM-III-R symptom criterion for generalized anxiety disorder. Moreover, analysis of the convergent validity of the Penn State Worry Questionnaire indicated that, for the subjects with generalized anxiety disorder, this measure was significantly correlated with the tension subscale of the Self-Analysis Questionnaire but not the anxiety and depression subscales. In an earlier study (43), the Penn State Worry Questionnaire was also not found to be correlated with measures of anxiety or depression (i.e., Hamilton scales, Beck Depression Inventory) in a group of patients with generalized anxiety disorder. In a recent study of 292 patients with anxiety or mood disorders (T.A. Brown et al., unpublished 1994 manuscript), symptom ratings from the motor tension cluster and the vigilance and scanning cluster were more strongly correlated with measures of generalized anxiety disorder (e.g., Penn State Worry Questionnaire, ratings of clinical severity of generalized anxiety disorder) than were ratings of symptoms from the autonomous hyperactivity cluster. Collectively, such findings support the revision of the associated symptom list in DSM-IV, which reduces the number of symptoms from 18 (DSM-III-R) to six (appendix 1).

ISSUES PERTAINING TO DSM-IV

For the reasons articulated in the preceding, the DSM-IV Anxiety Disorders Work Group ultimately recommended the continued placement of generalized anxiety disorder within the anxiety disorders, with revisions to the criteria set. The DSM-IV diagnostic criteria for generalized anxiety disorder are listed in appendix 1. Some of the more substantial revisions to these criteria, as guided by the data reviewed here, include the increased emphasis on the uncontrollability aspect of worry (criterion B) and the reduction of the associated symptom criterion (criterion C) to six symptoms (largely through the elimination of symptoms formerly constituting the autonomous hyperactivity cluster in DSM-III-R).

Although generalized anxiety disorder has been retained in DSM-IV, researchers should be aware that there are a number of unresolved issues surrounding the etiological basis for the diagnosis. The difficulties include the problems with diagnostic unreliability shown by recent studies using the DSM-III-R criteria. The kappa coefficients have been only in the fair range, which, interestingly, is more characteristic of personality disorders than other anxiety disorders. It is possible that the DSM-IV definitions may improve reliability, but there is no evidence yet that this will happen.

Second, generalized anxiety disorder as a principal diagnosis has been associated with extremely high rates of comorbidity. Whereas some additional diagnoses associated with generalized anxiety disorder (such as simple phobia) seem unrelated, the possibility remains that generalized anxiety disorder may be better conceptualized as a vulnerability to developing additional anxiety and, perhaps, mood disorders. In other words, in view of the seemingly earlier age at onset for this diagnosis that for other anxiety and mood disorders, generalized anxiety disorder, along with perhaps dysthymia and mixed anxiety-depression, may well be better conceptualized as a trait, as already noted, a general vulnerability.

Moreover, the difficulties that have been encountered with the validation of generalized anxiety disorder could be considered on a larger scale, namely, the validity of the DSM-III-R and DSM-IV classification systems for anxiety and mood disorders. Indeed, many researchers (47, 48) have raised the possibility that these classification systems are erroneously distinguishing phenomena on the basis of differing manifestations of a common pathophysiology. Evidence that is frequently offered in support of this argument includes findings that a variety of disorders respond favorably to antidepressant medication (47) and data relating to many of the issues raised in the present paper, such as high comorbidity and difficulties in differentiating the symptoms of anxiety and depression. Whereas more study of the biological commonalities and differences among the anxiety and mood disorders is needed (49), a substantial literature attesting to the distinct familial transmission of many of these disorders (e.g., panic disorder, simple phobia, social phobia) could be taken in support of the DSM nosology (50–52). In addition, findings suggesting that the anxiety and mood disorders respond similarly to pharmacological treatment could be considered tentative in the context of findings indicating distinctiveness in therapeutic response (53, 54).

On the other hand, generalized anxiety disorder at the syndromal level seems to be associated with relatively high levels of construct validity. That is, generalized anxiety disorder can be separated reasonably well from other anxiety disorders by means of psychometric evaluation. As with the other anxiety disorders, generalized anxiety disorder can be differentiated from major depression on the basis of its relative absence of anhedonia and low positive-affect (31, 55). The alterations in criteria for DSM-IV seem to have provided relatively firm boundaries with other anxiety disorders, as well as a threshold between this diagnosis and the absence of mental disorder. Moreover, the creation of new categories in DSM-IV that reflect subsyndromal disorders (e.g., mixed anxiety-depression, minor depression) may further augment the boundary for generalized anxiety disorder by providing a diagnosis for patients whose conditions lacked formal diagnostic coverage in DSM-III-R and who may have potentially diluted the generalized anxiety disorder category. In addition, some new data from family studies seem to support the criterion validity of generalized anxiety disorder, although these data are still relatively limited. Differences in age at onset and treatment response also point to a different kind of entity.

Perhaps the most interesting and substantial development has been the determination, now rather widely replicated, of a set of somatic symptoms associated with generalized anxiety disorder that is very different from those for other DSM-III-R anxiety disorders, such as panic disorder. The identification by diverse investigative groups of a core of somatic symptoms, formally found in the motor tension cluster and the vigilance and scanning cluster of the DSM-III-R associated symptom criterion, may well identify a truly unique syndrome that would have implications for the development of new and more effective pharmacological treatments.

Nonetheless, an important consequence of the process of evaluating and revising the diagnostic criteria for DSM-IV has been the explication and clarification of a variety of issues and lacunae in the empirical evidence on the nature and classification of disorders. Accordingly, in light of the issues discussed here, the DSM-IV criteria for generalized anxiety disorder should be heralded mainly for their heuristic value, as opposed to being viewed as a last statement on the nature of this disorder.

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**REFERENCES**


APPENDIX 1. DSM-IV Diagnostic Criteria for Generalized Anxiety Disorder

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not, for at least 6 months, about a number of events or activities (such as work or school performance).

B. The person finds it difficult to control the worry.

C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms present for more days than not for the past 6 months) . . . .

1. Restlessness or feeling keyed up or on edge
2. Being easily fatigued
3. Difficult concentrating or mind going blank
4. Irritability
5. Muscle tension
6. Sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)

D. The focus of the anxiety and worry is not confined to features of an Axis I disorder, e.g., the anxiety or worry is not about having a Panic Attack (as in Panic Disorder), being embarrassed in public (as in Social Phobia), being contaminated (as in Obsessive-Compulsive Disorder), being away from home or close relatives (as in Separation Anxiety Disorder), gaining weight (as in Anorexia Nervosa), having multiple physical complaints (as in Somatization Disorder), or having a serious illness (as in Hypochondriasis), and the anxiety and worry do not occur exclusively during Posttraumatic Stress Disorder.

E. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

F. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse) or a general medical condition (e.g., hyperthyroidism) and does not occur exclusively during a Mood Disorder, a Psychotic Disorder, or a Pervasive Developmental Disorder.


