

Frequency of Anxiety Disorders in Psychiatric Outpatients With Major Depressive Disorder

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Objective: The authors determined the frequency of anxiety disorders in a large group of depressed outpatients seeking treatment.

Method: The Structured Clinical Interview for DSM-IV was administered to 373 depressed outpatients.

Results: More than one-half of the patients met the full criteria for a current anxiety disorder, and more than one-half of

the patients with an anxiety disorder had more than one. When partial remissions and anxiety disorder diagnoses classified as “not otherwise specified” were included, two-thirds of the patients had a current anxiety disorder and three-quarters had a lifetime history of an anxiety disorder.

Conclusions: The majority of patients with a principal diagnosis of unipolar major depressive disorder have a comorbid anxiety disorder. Because antidepressant medications have differential efficacies for anxiety disorders, knowledge of the presence of a comorbid anxiety disorder in a depressed patient may have treatment implications.

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Numerous studies have shown that symptoms of anxiety are frequent in patients with major depressive disorder, and the presence of anxiety symptoms is associated with a more severe and chronic course (1–3). Most of the research examining the frequency of anxiety in depressed patients has focused on symptoms of anxiety. While there are several reports from epidemiological studies on the frequency of anxiety disorders in individuals with major depressive disorder (4, 5), there have been surprisingly few studies of the full

range of anxiety disorders in groups of depressed psychiatric patients. Sanderson and colleagues (6) examined anxiety disorder comorbidity among 197 patients with major depressive disorder seen in a center for cognitive therapy. Overall, 41.6% of the depressed patients had a comorbid anxiety disorder, the most frequent of which was generalized anxiety disorder. Some of the results of this study were surprising, e.g., the frequencies of some anxiety disorders, such as posttraumatic stress disorder (PTSD) and simple

TABLE 1. Rates of Current and Lifetime Anxiety Disorders in 373 Outpatients With Major Depressive Disorder

Anxiety Disorder	Current		Lifetime	
	N	%	N	%
Meeting full DSM-IV criteria				
Panic disorder without agoraphobia	11	2.9	15	4.0
Panic disorder with agoraphobia	53	14.2	72	19.3
Agoraphobia without panic disorder	4	1.1	5	1.3
Specific phobia	51	13.7	56	15.0
Social phobia	123	33.0	133	35.7
Obsessive-compulsive disorder	37	9.9	47	12.6
Posttraumatic stress disorder	50	13.4	90	24.1
Acute stress disorder	1	0.3	3	0.8
Generalized anxiety disorder	56	15.0	56	15.0
Anxiety due to a general medical condition	0	0.0	0	0.0
Any anxiety disorder	214	57.4	245	65.7
In partial remission				
Panic disorder without agoraphobia	3	0.8	3	0.8
Panic disorder with agoraphobia	6	1.6	6	1.6
Agoraphobia without panic disorder	0	0.0	0	0.0
Specific phobia	1	0.3	1	0.3
Social phobia	0	0.0	0	0.0
Obsessive-compulsive disorder	0	0.0	0	0.0
Posttraumatic stress disorder	31	8.3	31	8.3
Acute stress disorder	0	0.0	0	0.0
Generalized anxiety disorder	0	0.0	0	0.0
Anxiety due to a general medical condition	0	0.0	0	0.0
Any anxiety disorder in partial remission	40	10.7	40	10.7
Not otherwise specified				
Subthreshold panic disorder	8	2.1	9	2.4
Subthreshold specific phobia	2	0.5	2	0.5
Subthreshold social phobia	3	0.8	4	1.1
Subthreshold obsessive-compulsive disorder	2	0.5	2	0.5
Subthreshold posttraumatic stress disorder	35	9.4	43	11.5
Subthreshold generalized anxiety disorder	6	1.6	6	1.6
Mixed anxiety-depressive disorder	0	0.0	0	0.0
Other anxiety disorder	4	1.1	4	1.1
Any anxiety disorder not otherwise specified	57	15.3	67	18.0

phobia, were lower than the prevalence rates reported in epidemiological surveys of the general population.

In the present study, part of the Rhode Island Methods to Improve Diagnostic Assessment and Services project, we examined the frequency of DSM-IV anxiety disorders in a large cohort of depressed outpatients seen in an outpatient psychiatric practice. Our emphasis here is on the frequency of current DSM-IV anxiety disorders, although we also report lifetime prevalence rates so that our results can be compared with those from studies that exclusively focused on lifetime rates. We report the frequency of each of the 10 DSM-IV anxiety disorders defined by specific inclusion and exclusion criteria and the residual category of anxiety disorder not otherwise specified.

Method

One thousand psychiatric outpatients in the Rhode Island Hospital Department of Psychiatry outpatient practice were evaluated with the Structured Clinical Interview for DSM-IV (SCID-I) (7). The Rhode Island Hospital institutional review committee approved the research protocol, and all patients provided informed, written consent. As described elsewhere (8), the patients who did and did not participate in the study were similar in gender, education, marital status, and scores on self-administered symptom questionnaires.

Eight diagnostic raters were used to administer the SCID. The raters included the authors of the paper, each of whom has extensive experience administering research diagnostic interviews. The other five raters were doctorate-level psychologists or research assistants with college degrees in the social or biological sciences. All raters received 3 months of training, during which they observed at least 20 interviews, and they were observed and supervised in their administration of 20 evaluations. At the end of the training period the raters were required to demonstrate exact, or nearly exact, agreement with a senior diagnostician on five consecutive evaluations. During the course of the study, information on the diagnostic reliability of joint interviews was collected on 26 patients. For mood and anxiety disorders diagnosed in at least two patients by at least one of the raters, the kappa coefficients were as follows: major depressive disorder, 1.00; dysthymic disorder, 1.00; bipolar disorder, 1.00; depressive disorder not otherwise specified, 0.45; panic disorder, 1.00; social phobia, 0.87; obsessive-compulsive disorder (OCD), 1.00; specific phobia, 1.00; generalized anxiety disorder, 0.64; PTSD, 1.00; and anxiety disorder not otherwise specified, 0.19.

"Not otherwise specified" diagnoses were made in two ways. First, these diagnoses were made for patients with clinically significant symptoms that fell below the DSM-IV threshold for the diagnosis of a specific disorder. In such cases we indicated which anxiety disorder the not-otherwise-specified diagnosis was related to (e.g., subthreshold panic disorder, subthreshold PTSD, etc.). The second circumstance in which a patient was given a current not-otherwise-specified diagnosis was when the full DSM-IV criteria for a disorder had been met in the past, but the symptoms had partially but not completely remitted. Although DSM-IV provides specific guidelines regarding use of a partial-remission specifier only for the mood and substance use disorders, we adopted this specifier for all disorders. For example, someone who met the DSM-IV criteria for PTSD 5 years ago but at the time of the evaluation was bothered by a subthreshold number of criteria would have been diagnosed with the disorder in partial remission. We examined the impact of both methods of making not-otherwise-specified diagnoses on the overall estimate of the frequency of anxiety disorders in depressed patients.

Results

A total of 373 patients presented with a chief complaint of depression and were given a principal diagnosis of unipolar major depressive disorder. The group included 123 men (33.0%) and 250 women (67.0%), who ranged in age from 18 to 76 years (mean=39.6, SD=12.30). Nearly one-half of the subjects were married (N=166, 44.5%); the remainder were single (N=96, 25.7%), divorced (N=60, 16.1%), separated (N=33, 8.8%), widowed (N=6, 1.6%), or living with someone as if in a marital relationship (N=12, 3.2%). About two-thirds (N=245) had high school degrees or equivalency, 12.1% (N=45) had not graduated from high school, and 22.3% (N=83) had graduated from a 4-year college or university. The study group was predominantly white (84.5%, N=315). The patients' mean score on the Global Assessment of Functioning was 49.8 (SD=9.1). More than one-half of the patients had experienced at least one prior episode of major depressive disorder (N=194, 52.0%), and the median duration of the current episode was 50 weeks.

The data in Table 1 show the frequency of current and lifetime anxiety disorders in the 373 outpatients with a

principal diagnosis of unipolar major depressive disorder. At the time of the evaluation, 57.4% (N=214) of the patients met the criteria for one of the 10 specific anxiety disorders. Including patients with an anxiety disorder in partial remission increased the frequency to 60.6% (N=226). Adding the patients with an anxiety disorder not otherwise specified to this group increased the percentage of patients with at least one current anxiety disorder to 67.6% (N=252). The lifetime frequency of any anxiety disorder (including not-otherwise-specified diagnoses) was 74.0% (N=276).

For the entire study group the mean number of current anxiety disorders, including those in partial remission and not-otherwise-specified disorders, was 1.31 (SD=1.2). The majority of patients with an anxiety disorder had more than one (57.1%, 144 of 252). When the partially remitted and not-otherwise-specified disorders were not included, the mean number of anxiety disorder diagnoses decreased to 1.03 (SD=1.1), although nearly the same percentage of patients with an anxiety disorder had two or more diagnoses (54.2%, 116 of 214).

The most frequent current anxiety disorder was social phobia, diagnosed in one-third of the patients. Panic disorder, specific phobia, PTSD, and generalized anxiety disorder were each diagnosed in approximately 15% of the patients. Forty patients (10.7%) were diagnosed with a disorder in partial remission, and 57 (15.3%) received a current not-otherwise-specified diagnosis. PTSD was the most frequent partially remitted and subthreshold disorder.

Discussion

Anxiety disorders are frequent in depressed outpatients seeking treatment, although the overall frequency of any anxiety disorder depends, in part, on the breadth of the assessment. More than one-half of the depressed patients in this study met the full DSM-IV criteria for a specific anxiety disorder; when not-otherwise-specified diagnoses were included, two-thirds of the depressed patients had an anxiety disorder. Of the depressed patients with an anxiety disorder, one-half had more than one. These results highlight the importance of conducting thorough diagnostic evaluations of outpatients with a chief complaint of depression.

The presence of a comorbid anxiety disorder can have treatment implications. It is generally believed that all antidepressant medications are approximately equally effective for the treatment of depression. However, these medications are not equally effective in the treatment of anxiety disorders. For example, the serotonin reuptake inhibitors are more effective than tricyclic antidepressants in the treatment of OCD, and monoamine oxidase inhibitors may be more effective than tricyclic antidepressants in treating social phobia (9, 10). Several antidepressant medications are indicated for the treatment of certain anxiety disorders, whereas other antidepressants have not been

consistently shown to also be effective in treating anxiety disorders. Certain medications have acquired a reputation of being more or less anxiogenic or anxiolytic than others, and pharmaceutical companies have developed promotional campaigns suggesting that some medications are particularly well suited for treating depressed patients with anxious features. While knowledge of the presence of an anxiety disorder in a depressed patient might influence the choice of medication prescribed, there are, in fact, few data to support suggestions that depressed patients with anxious features respond differentially to the range of antidepressant medications.

Awareness of the presence of a comorbid anxiety disorder might also influence the prescription of psychotherapy. For example, cognitive behavior therapy has been demonstrated to be effective in the treatment of all of the specific anxiety disorders. Interpersonal or psychodynamic therapy might also be effective in treating anxiety disorders. If a comorbid anxiety disorder is not appropriately recognized, patients might not receive these potentially effective forms of treatment. To our knowledge, there have been no controlled trials comparing the efficacy of medications and psychotherapy in the treatment of comorbid anxiety disorders in depressed patients. In light of the high prevalence of anxiety disorders among depressed patients, this line of research warrants attention. If one form of treatment proves superior to the other, or if the combination of both treatments produces the greatest improvement, then improved clinical detection of anxiety disorders in depressed patients might improve outcome by virtue of more appropriate treatment planning.

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References

1. Clayton PJ, Grove WM, Coryell W, Keller M, Hirschfeld R, Fawcett J: Follow-up and family study of anxious depression. *Am J Psychiatry* 1991; 148:1512-1517
2. Coryell W, Endicott J, Andreasen NC, Keller MB, Clayton PJ, Hirschfeld RM, Scheftner WA, Winokur G: Depression and panic attacks: the significance of overlap as reflected in follow-up and family study data. *Am J Psychiatry* 1988; 145: 293-300
3. Van Valkenburg C, Akiskal HS, Puzantian V, Rosenthal T: Anxious depressions: clinical, family history, and naturalistic outcome-comparisons with panic and major depressive disorders. *J Affect Disord* 1984; 6:67-82
4. Boyd JH, Burke JD, Gruenberg E, Holzer CE, Rae DS, George LK, Karno M, Stoltzman R, McEvoy L, Nestadt G: Exclusion criteria of DSM-III: a study of co-occurrence of hierarchy-free syndromes. *Arch Gen Psychiatry* 1984; 41:983-989

5. Kessler RC, Stang PE, Wittchen H-U, Ustun TB, Roy-Burne PP, Walters EE: Lifetime panic-depression comorbidity in the National Comorbidity Survey. *Arch Gen Psychiatry* 1998; 55: 801–808
6. Sanderson WC, Beck AT, Beck J: Syndrome comorbidity in patients with major depression or dysthymia: prevalence and temporal relationships. *Am J Psychiatry* 1990; 147: 1025–1028
7. First MB, Spitzer RL, Gibbon M, Williams JBW: Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Administration Booklet. Washington, DC, American Psychiatric Press, 1997
8. Zimmerman M, Mattia JI: Psychiatric diagnosis in clinical practice: is comorbidity being missed? *Compr Psychiatry* 1999; 40:182–191
9. Goodman WK, Price LH, Delgado PL, Palumbo J, Krystal JH, Nagy LM, Rasmussen SA, Heninger GR, Charney DS: Specificity of serotonin reuptake inhibitors in the treatment of obsessive-compulsive disorder: comparison of fluvoxamine and desipramine. *Arch Gen Psychiatry* 1990; 47:577–585
10. Simpson HB, Schneier FR, Campeas RB, Marshall RD, Fallon BA, Davies S, Klein DF, Liebowitz MR: Imipramine in the treatment of social phobia. *J Clin Psychopharmacol* 1998; 18:132–135