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Current and Lifetime Comorbidity of the *DSM–IV* Anxiety and Mood Disorders in a Large Clinical Sample

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The comorbidity of current and lifetime *DSM–IV* anxiety and mood disorders was examined in 1,127 outpatients who were assessed with the Anxiety Disorders Interview Schedule for *DSM–IV:* Lifetime version (ADIS–IV–L). The current and lifetime prevalence of additional Axis I disorders in principal anxiety and mood disorders was found to be 57% and 81%, respectively. The principal diagnostic categories associated with the highest comorbidity rates were mood disorders, posttraumatic stress disorder (PTSD), and generalized anxiety disorder (GAD). A high rate of lifetime comorbidity was found between the anxiety and mood disorders; the lifetime association with mood disorders was particularly strong for PTSD, GAD, obsessive–compulsive disorder, and social phobia. The findings are discussed in regard to their implications for the classification of emotional disorders.

Diagnostic comorbidity refers to the co-occurrence of two or more current or lifetime mental disorders in the same individual. Although large-scale clinical and community studies of the diagnostic comorbidity of anxiety and mood disorders have only appeared over the past decade (e.g., T.A. Brown & Barlow, 1992; Kessler et al., 1996; Wittchen, Zhao, Kessler, & Eaton, 1994), findings have consistently shown that these disorders rarely present in isolation of other conditions. In studies of outpatient clinical samples, over 50% of patients with a principal *DSM–III–R* anxiety disorder have one or more additional diagnoses at the time of assessment (Brawman-Mintzer et al., 1993; T. A. Brown & Barlow, 1992; Sanderson, Di Nardo, Rapee, & Barlow, 1990). Similar results have been obtained in patients with *DSM–III–R* mood disorders: Both clinical and community studies have found that over half of patients with major depressive disorder meet diagnostic criteria for one or more current or lifetime anxiety disorders (e.g., T. A. Brown & Barlow, 1992; Kessler et al., 1996).

The results of such studies have far-ranging implications. From the perspective of the course and prognosis of disorders, the presence of comorbid anxiety and mood disorders has been linked to such variables as chronicity and severity of psychopathology, treatment outcome and relapse, treatment seeking, suicide potential, and overall psychosocial functioning (e.g., Bronisch & Wittchen, 1994; C. Brown, Schulberg, Madonia, & Shear, 1996; T. A. Brown, Antony, & Barlow, 1995; Magee, Eaton, Wittchen, McGonagle, & Kessler, 1996; Reich, Warshaw, Peterson, & White, 1993; Rohde, Lewinsohn, & Seeley, 1991). Moreover, high anxiety and mood disorder comorbidity has strong implications for the classification of emotional disorders (T. A. Brown, 1996; Clark, Watson, & Reynolds, 1995; Mineka, Watson, & Clark, 1998). With publication of the 4th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM–IV*, American Psychiatric Association, 1994), there now exist 12 anxiety disorder and 9 mood disorder categories, a dramatic increase over prior versions of the *DSM* (e.g., only 3 anxiety disorders existed in the 2nd edition of the *DSM*; American Psychiatric Association, 1968). Although implying greater precision in the classification of psychopathology, this expansion may have severely compromised the discriminant validity of *DSM* disorders (Andrews, 1996; T. A. Brown, 1996; Clark et al., 1995); specifically, the diagnostic system may be erroneously distinguishing conditions that are minor variations of broader underlying syndromes (Blashfield, 1990; Frances, Widiger, & Fyer, 1990). Consistent findings of high co-occurrence of anxiety and mood disorders could support this concern.

Particularly reflective of this argument are comorbidity findings involving *DSM–III–R* generalized anxiety disorder (GAD). In clinical samples, over 80% of patients with a principal diagnosis of GAD have at least one additional current anxiety or mood disorder diagnosis (Brawman-Mintzer et al., 1993; T. A. Brown & Barlow, 1992; Massion, Warshaw, & Keller, 1993); in an epidemiological sample, the lifetime comorbidity rate was 90% in persons with a history of GAD (Wittchen et al., 1994). Findings that comorbid GAD often remits with psychosocial treatment of another anxiety disorder also point to a possible lack of independence of this diagnosis (T. A. Brown, Antony, & Barlow, 1995). These data, in tandem with evidence of low diagnostic reliability (e.g., Di Nardo, Moras, Barlow, Rapee, & Brown, 1993), led to debate among researchers as to whether there was sufficient evidence of discriminant validity to retain GAD as a formal diagnostic category in *DSM–IV* (T. A. Brown, Barlow, & Liebowitz, 1994). Recent evidence at the diagnostic and symptom level suggests that the mood disorders may especially pose boundary problems for GAD (T. A. Brown, Chorpita, & Barlow, 1998; T. A. Brown, Di Nardo, Lehman, & Campbell, 2001; T. A. Brown, Marten, & Barlow,

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1995; Starcevic, 1995). Although GAD remained a formal diagnosis in *DSM–IV*, its diagnostic criteria were revised substantially in an effort to define its boundary in relation to conditions such as mood and adjustment disorders, other anxiety disorders, and nonpathological worry (T. A. Brown et al., 1994).

In addition to signifying the erroneous splitting of broader underlying syndromes, findings of high diagnostic comorbidity could indicate unnecessary overlap in definitional criteria or other artifacts such as the high base rates of some disorders such as social phobia (Frances et al., 1990). Other explanations include the possibility that emotional disorders co-occur because they emerge from the same genetic, biological, or psychosocial diatheses but that this shared vulnerability is manifested heterogeneously (i.e., as different *DSM* disorders) as a function of exposure to differing environmental influences, other genetic/biologic factors, and so on. For instance, findings from a large-scale twin study indicate that whereas a clear genetic influence exists in GAD, the genetic factors in GAD are completely shared with major depression. However, although GAD and major depression share genetic influences, their environmental determinants are mostly distinct (Kendler, Neale, Kessler, Heath, & Eaves, 1992; Roy, Neale, Pedersen, Mathé, & Kendler, 1995). Recent evidence and conceptualization based on the tripartite model of anxiety and depression (Clark & Watson, 1991) are in accord with this position. In addition to accounting for the overlap in anxiety and mood disorders, the trait of negative affect (and possibly positive affect in the case of mood disorders and social phobia) may exert strong influence on the etiology and course of these conditions (cf. T. A. Brown et al., 1998; Clark, Watson, & Mineka, 1994; Mineka et al., 1998).

Moreover, comorbidity may partly stem from the key features of an emotional disorder that serve as risk factors for the development of other diagnoses. For example, consistent with descriptive findings based on *DSM–III–R* definitions (T. A. Brown & Barlow, 1992), the rate of mood disorders may increase in patients with panic disorder as a function of increasing levels of agoraphobic avoidance (i.e., restrictions in mobility result in reduced participation in pleasurable activities and a sense of hopelessness, leading to mood disorder). Substance use disorders may be more frequently comorbid with disorders characterized by chronically high levels of autonomic arousal (e.g., panic disorder, posttraumatic stress disorder) due to heightened motivation to alleviate these aversive symptoms (Kushner, Sher, & Beitman, 1990). Yet, such findings may reflect the existence of a more nonspecific severity dimension that accounts for the intensity of a given disorder (e.g., severity of agoraphobia, and panic attacks in panic disorder) as well as for the number and severity of co-occurring symptoms and disorders (Blashfield, 1990).

With these issues in mind, the aim of the present study was to evaluate the rates and patterns of diagnostic comorbidity in a large outpatient sample. In addition to being the first large-scale clinical study of comorbidity using *DSM–IV* criteria, this investigation is a substantial extension over our *DSM–III–R* study with regard to sample size (i.e., N = 1,127 vs. 468 in T. A. Brown & Barlow, 1992), improved diagnostic reliability (see Method; T. A. Brown et al., 2001), and focus on current and lifetime disorders. Of particular interest was determination of possible differential aggregations of anxiety disorders with mood disorders, changes in comorbidity estimates across *DSM–III–R* and *DSM–IV*, and variations in comorbidity rates in current versus lifetime disorders. In addition, the study's assessment methods permitted reliable determination of patients' principal diagnoses (T. A. Brown et al., 2001)—the current diagnosis associated with the most distress and impairment (cf. American Psychiatric Association, 1994, p. 3). Although usually not conducted in epidemiological studies, analysis of comorbidity by principal diagnosis is important for several reasons, for example, informing treatment outcome and psychopathology studies (whose enrollment criteria typically select for principal diagnoses) and providing a more complete and accurate description of the aggregation of emotional disorders.

Method

Participants

Participants were 1,127 patients presenting for assessment and treatment at the Center for Stress and Anxiety Disorders, University at Albany, State University of New York (n = 412), and the Center for Anxiety and Related Disorders, Boston University (n = 715).[1] Women constituted the larger portion of the sample (62%); average age was 33.94 years (SD = 10.89 years, range = 18–64). The racial/ethnic breakdown of the sample was as follows: Caucasian (88%), African American (3%), Hispanic (3%), Asian (3%), other (1%), and missing (2%).

Patients met several inclusion and exclusion criteria that were assessed by initial telephone screening and reassessed and confirmed during the diagnostic interviews. Specifically, patients were between the ages of 18 and 65 and had a presenting complaint involving an anxiety or mood disorder. Patients were excluded if any of the following were present: (a) current hallucinations or delusions; (b) current or recent (within past 6 months) alcohol or substance abuse or dependence; (c) current suicidal or homicidal risk meriting crisis intervention; and (d) two or more hospitalizations in the past 5 years for psychotic symptoms. Patients were also required to meet psychotropic medication and psychotherapy stabilization criteria for the periods preceding and overlapping with the diagnostic assessment. Patients using anxiolytics and beta-blockers were required to maintain the same dosage for at least 1 month. Patients on antidepressants (tricyclics, serotonin-specific re-uptake inhibitors, monoamine oxidase inhibitors) had to maintain a stable dosage for at least 3 months. For patients in the process of discontinuing medications, the wash-out period was 1 month for all drugs (i.e., period since last dose taken). Patients in psychotherapy for an emotional problem were required to remain in the same therapeutic relationship for at least 3 months; the psychotherapy wash-out period was a minimum of 1 month since the final therapy session.

Anxiety Disorder Interview Schedule for DSM–IV: Lifetime Version (ADIS–IV–L; Di Nardo, Brown, & Barlow, 1994)

The *ADIS–IV–L* is a semistructured interview designed to establish reliable diagnosis of the *DSM–IV* anxiety, mood, somatoform, and substance use disorders and to screen for the presence of other conditions (e.g., psychotic disorders). The *ADIS–IV–L* represents a substantial revision of the Anxiety Disorders Interview Schedule-Revised (Di Nardo & Barlow, 1988). In addition to being updated for *DSM–IV* diagnostic criteria, revisions introduced in the *ADIS–IV–L* include the assessment of lifetime disorders, dimensional assessment (0–8 ratings) of key and associated features of most disorders, and a diagnostic timeline intended to foster accurate determination of the onset, remission, and temporal sequence of

[1] Our research center relocated from the State University of New York at Albany to Boston University in September 1996.

current and lifetime disorders. Although the instrument's name suggests a predominant emphasis on anxiety disorders, the *ADIS–IV–L* diagnostic sections for current and lifetime mood, substance use, and somatoform disorders are equally detailed (e.g., dimensional ratings of constituent key and associated symptoms and distress/impairment; items fostering differential diagnosis with neighboring conditions; inquiry on precipitants and life stressors at the time of disorder onset; reasons for remission); in fact, the detailed inquiry in these sections exceeds that found in other popular instruments such as the Structured Clinical Interview for *DSM–IV* (SCID; First, Spitzer, Gibbon, & Williams, 1997).[2]

For each current and lifetime diagnosis, interviewers assigned a 0–8 clinical severity rating (CSR) that indicated their judgment of the degree of distress and impairment associated with the disorder (0 = *none,* 8 = *very severely disturbing/disabling*). For outpatients assigned two or more current diagnoses, the "principal" diagnosis was the one receiving the highest CSR. For current and lifetime disorders that met or surpassed the threshold for a formal *DSM–IV* diagnosis, CSRs of 4 (*definitely disturbing/disabling*) or higher were assigned (*clinical* diagnoses). Current clinical diagnoses not deemed to be the principal diagnosis are referred to as *additional* diagnoses.

Diagnosticians were 6 clinical psychologists and 30 advanced clinical doctoral students. To participate in the study, diagnosticians underwent extensive training and met strict certification criteria in the administration of the *ADIS–IV–L* (see T. A. Brown et al., 2001, for a detailed description of these procedures). A reliability study of a subset of the current sample (N = 362) who had two independent administrations of the *ADIS–IV–L* indicated good-to-excellent interrater agreement for current disorders (range of κs = .67–.86) and lifetime disorders (range of κs = .58–.83) except dysthymia (e.g., κ = .36 as a lifetime diagnosis; T. A. Brown et al., 2001).

Results

Comorbidity in Principal DSM–IV Anxiety and Mood Disorders

Current additional diagnoses. Table 1 presents the rates and patterns of current additional diagnoses for patients with current principal *DSM–IV* diagnoses (N = 968)[3] of panic disorder (PD), panic disorder with agoraphobia (PDA), social phobia (SOC), generalized anxiety disorder (GAD), obsessive–compulsive disorder (OCD), specific phobia (SPEC), posttraumatic stress disorder (PTSD), major depressive disorder (MDD), and dysthymia (DYS). As seen in Table 1, comorbid diagnoses were quite common—57% of the patients with these principal anxiety or mood disorders had at least one additional Axis I diagnosis at the time of the evaluation. Additional anxiety disorders and mood disorders were evident in 43% and 28% of patients, respectively (the combined comorbidity rate of one or more additional anxiety or mood disorders was 55%). The most common additional diagnoses were SOC (22%), MDD (20%), GAD (13%), and SPEC (13%). However, for purposes of ongoing studies on the diagnostic boundary between GAD and the mood disorders, *ADIS–IV–L* interviewers indicated cases in which all of the *DSM–IV* criteria for GAD were met except for the diagnostic hierarchy rule stating that the diagnosis should not be assigned if its features occur during the course of a mood disorder. When these cases were included (indicated as "GAD: no hierarchy" in the tables), GAD was the most common additional diagnosis (25%).[4]

A chi-square analysis indicated that the principal diagnostic categories differed significantly in the rates of Axis I comorbidity (i.e., any Axis I disorder), $\chi^2(8, N = 968) = 60.43, p < .001$. Odds ratios (OR; 95% confidence intervals) indicated that the principal diagnoses associated with significantly elevated risk for Axis I comorbidity were PTSD (92%, OR = 1.64), DYS (76%, OR = 1.36; although estimates and significance testing for principal PTSD and DYS should be interpreted with caution because of their low occurrence in the sample), MDD (69%, OR = 1.25), GAD (68%, OR = 1.24), and PDA (62%, OR = 1.14). The principal diagnoses with the lowest overall comorbidity rates were SPEC (34%), PD (42%), and SOC (46%), although OR analyses indicated that only SOC and SPEC were associated with significantly decreased risk of Axis I comorbidity.

The principal diagnoses also differed in their comorbidity rates with additional anxiety disorders, $\chi^2(8, N = 968) = 53.97, p < .001$. Principal diagnoses associated with heightened risk of comorbid anxiety disorders were MDD (64%, OR = 1.58), GAD (52%, OR = 1.25), and PDA (47%, OR = 1.17). Current anxiety disorder comorbidity was also quite high in principal PTSD (62%) and DYS (57%), although ORs failed to reach statistical significance. Significantly lower risk of anxiety disorder comorbidity was noted for SPEC (27%, OR = .61) and SOC (28%, OR = .61).

Collapsing across all principal anxiety disorders, 30% of patients had an additional mood disorder at the time of the evaluation. The rates of additional mood disorders differed significantly across the nine principal diagnostic groups, $\chi^2(8, N = 968) = 56.23, p < .001$. Three principal diagnoses had significantly increased rates of mood disorders: PTSD (77%, OR = 2.79), GAD (36%, OR = 1.32), and PDA (33%, OR = 1.28). The principal diagnosis of SPEC had a significantly lower likelihood of comorbid mood disorders (10%, OR = .34).

With regard to panic disorder, we expected that the presence of agoraphobic avoidance (PDA) would be associated with higher overall comorbidity and comorbidity with mood disorders than panic disorder without agoraphobia (PD). As seen in Table 1, this prediction was confirmed by the significant ORs for PDA (range of ORs = 1.14–1.28), whereas the principal diagnosis of PD was associated with a nonsignificant decreased risk of comorbidity (range of ORs = .58–.84).

Although descriptive findings are presented in Table 1, inferential statistical comparisons involving specific comorbid diagnoses were not conducted because of absence of explicit hypothesis

[2] Although the title of the ADIS was apt when the interview was first developed in the early 1980s, its historical name is now inaccurate and masks the in-depth and reliable diagnostic coverage currently provided for current and past mood, somatoform, and substance use disorders (e.g., κ = .83 for lifetime alcohol use disorders; T. A. Brown et al., 2001). For this reason, it is likely that the ADIS–IV–L will be renamed in its next version, a revision that will also include further extensions to its diagnostic coverage (e.g., trichotillomania).

[3] The sample size for the analyses for principal diagnoses was reduced to 968 because of the elimination of cases with coprincipal diagnoses (n = 102) and cases with principal diagnoses other than the major anxiety and mood disorder categories (e.g., anxiety or depressive disorder not otherwise specified; n = 57).

[4] In an analysis using the sample from T. A. Brown et al. (2001) of 362 patients who underwent two independent administrations of the *ADIS–IV–L*, good interrater reliability was found for GAD, including cases in which the *DSM–IV* hierarchy rule with mood disorders was lifted (κ = .72).

Table 1
Percentages (and Odds Ratios) of Current Additional Diagnoses in Patients With Current Principal Anxiety and Mood Disorders (N = 968)

Current additional diagnosis	*DSM–IV* principal diagnosis (*n*)											
	PD (36)	PDA (324)	PD/A (360)	SOC (186)	GAD (120)	OCD (77)	SPEC (110)	PTSD (13)	MDD (81)	DYS (21)	MDD/DYS (102)	Overall[a]
Any Axis I	42	62	60	46	68	57	34	92	69	76	71	57
	(.73)	(1.14*)	(1.09)	(.78*)	(1.24*)	(1.01)	(.56*)	(1.64*)	(1.25*)	(1.36*)	(1.28*)	
Any anxiety/mood	42	60	59	45	65	53	33	92	68	76	70	55
	(.75)	(1.16*)	(1.12)	(.79*)	(1.21*)	(.96)	(.56*)	(1.69*)	(1.26*)	(1.40*)	(1.30*)	
Any anxiety disorder	36	47	46	28	52	39	27	62	64	57	63	43
	(.84)	(1.17*)	(1.14)	(.61*)	(1.25*)	(.91)	(.61*)	(1.45)	(1.58*)	(1.35)	(1.56*)	
Any mood disorder	17	33	31	29	36	32	10	77	11	38	17	28
	(.58)	(1.28*)	(1.19)	(1.04)	(1.32*)	(1.17)	(.34*)	(2.79*)	(.37*)	(1.36)	(.56*)	
Anxiety disorders												
PD	—	—	—	1	3	1	0	0	4	0	3	1
				(.28)	(3.25)	(.86)	(—)	(—)	(3.25)	(—)	(2.48)	
PDA	—	—	—	3	15	8	5	23	15	14	15	9
				(.24*)	(2.09*)	(.88)	(.58)	(2.75)	(1.90*)	(1.68)	(1.96*)	
PD or PDA	—	—	—	3	18	9	5	23	19	14	18	10
				(.24*)	(2.24*)	(.88)	(.49)	(2.33)	(2.08*)	(1.42)	(2.03*)	
SOC	8	15	15	—	36	26	9	15	41	48	42	22
	(.37)	(.58*)	(.53*)		(2.33*)	(1.21)	(.38*)	(.70)	(2.07*)	(2.25*)	(2.24*)	
GAD	19	16	16	13	—	12	5	23	5	5	5	13
	(1.59)	(1.50*)	(1.64*)	(1.10)		(.93)	(.40*)	(1.87)	(.37*)	(.38)	(.36*)	
GAD: No hierarchy	22	22	22	21	—	16	7	38	67	90	72	25
	(.87)	(.79)	(.78*)	(.78)		(.59)	(.26*)	(1.52)	(3.16*)	(3.80*)	(3.73*)	
OCD	6	7	7	8	4	—	3	23	9	5	8	7
	(.83)	(1.12)	(1.08)	(1.29)	(.59)		(.38)	(3.62*)	(1.35)	(.71)	(1.21)	
SPEC	8	15	15	8	12	12	15[b]	15	15	10	14	13
	(.65)	(1.36)	(1.28)	(.58*)	(.91)	(.91)	(1.17)	(1.21)	(1.18)	(.75)	(1.09)	
PTSD	0	4	4	3	1	0	0	—	6	0	5	3
	(—)	(2.30*)	(1.95)	(1.09)	(.30)	(—)	(—)		(2.84*)	(—)	(2.20)	
Other anxiety	3	4	4	3	1	3	3	0	2	0	2	3
	(.92)	(1.86)	(1.81)	(1.10)	(.25)	(.86)	(.90)	(—)	(.81)	(—)	(.63)	
Mood disorders												
MDD	8	24	23	14	26	22	3	69	—	33	—	20
	(.41)	(1.41*)	(1.28)	(.66*)	(1.39)	(1.14)	(.12*)	(3.67*)		(1.73)		
DYS	8	7	7	13	6	10	4	23	11	—	—	8
	(.99)	(.73)	(.74)	(1.75*)	(.66)	(1.26)	(.40)	(2.80*)	(1.36)			
Other mood	3	3	3	5	6	4	4	0	0	5	1	4
	(.74)	(.87)	(.84)	(1.40)	(1.71)	(1.05)	(.98)	(—)	(—)	(1.29)	(.24)	
Other disorders												
Somatoform	0	2	1	1	4	1	0	0	2	0	2	2
	(—)	(.99)	(.84)	(.65)	(3.53*)	(.83)	(—)	(—)	(1.68)	(—)	(1.31)	
Other Axis I	3	2	2	1	6	6	2	0	6	0	5	3
	(.92)	(.63)	(.64)	(.31)	(2.25)	(2.41)	(.58)	(—)	(2.28)	(—)	(1.77)	

Note. *DSM–IV* = *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition (American Psychiatric Association, 1994); PD = panic disorder; PDA = panic disorder with agoraphobia; PD/A = PD or PDA; SOC = social phobia; GAD = generalized anxiety disorder; GAD: No hierarchy = GAD ignoring *DSM–IV* hierarchy rule with mood disorders; OCD = obsessive–compulsive disorder; SPEC = specific phobia; PTSD = posttraumatic stress disorder; MDD = major depressive disorder; DYS = dysthymia; MDD/DYS = MDD or DYS. Dashes in parentheses indicate that the odds ratio is inapplicable.

[a] Overall frequency category was assigned as an additional diagnosis; [b] In Tables 1–4, percentages in the diagonal for SPEC indicate rates of comorbid specific phobia types (e.g., 15% of patients with principal SPEC had additional SPECs at the time of the evaluation).

* Significantly increased or decreased risk of co-occurring disorder (95% confidence interval).

testing, Type I error issues, and so forth. Nonetheless, a few aspects of these results are noteworthy. The principal diagnoses of MDD and DYS had the highest rates of comorbid SOC (41% and 48%, respectively). When *DSM–IV* hierarchy rules were adhered to strictly, GAD occurred infrequently (5%) as an additional diagnosis for principal MDD and DYS (in fact, MDD was associated with decreased risk of GAD, OR = .37). However, when ignoring the rule stating that GAD cannot be assigned if its features occur during a mood disorder, GAD was highly comorbid with MDD and DYS (67%, OR = 3.16, and 90%, OR = 3.80, respectively). In other words, two thirds of the patients with principal MDD, and virtually all patients with principal DYS, would have been assigned an additional diagnosis of GAD had it not been for this *DSM–IV* hierarchy rule. Although current somatoform disorders occurred infrequently in the sample (2%), the principal diagnosis of GAD was associated with an over threefold risk of these

conditions (4%, OR = 3.53). Finally, the only two principal diagnoses to be associated with significantly elevated risk of current PTSD were MDD (69%, OR = 3.67) and PDA (24%, OR = 1.41).

Additional lifetime diagnoses. Table 2 presents the rates and patterns of lifetime comorbid diagnoses (when current and past additional diagnoses were collapsed) for patients with current principal anxiety and mood disorders. As expected, comorbidity T2

Table 2
Percentages (and Odds Ratios) of Additional Lifetime Diagnoses in Patients With Current Principal Anxiety and Mood Disorders (N = 968)

	DSM–IV principal diagnosis (*n*)											
Lifetime additional diagnosis	PD (36)	PDA (324)	PD/A (360)	SOC (186)	GAD (120)	OCD (77)	SPEC (110)	PTSD (13)	MDD (81)	DYS (21)	MDD/DYS (102)	Overall[a]
Any Axis I	75	82	81	72	92	86	65	100	91	100	93	81
	(.93)	(1.03)	(1.01)	(.86*)	(1.16*)	(1.07)	(.78*)	(1.24*)	(1.15*)	(1.25*)	(1.18*)	
Any anxiety/mood	69	77	76	67	88	83	56	100	90	100	92	76
	(.91)	(1.01)	(1.00)	(.86*)	(1.19*)	(1.10)	(.72*)	(1.32*)	(1.20*)	(1.32*)	(1.24*)	
Any anxiety disorder	53	56	56	37	71	45	45	69	73	62	71	54
	(.98)	(1.07)	(1.07)	(.63*)	(1.38*)	(.84)	(.81)	(1.30)	(1.40*)	(1.16)	(1.37*)	
Any mood disorder	44	60	59	57	73	71	36	85	57	76	61	59
	(.74)	(1.03)	(.99)	(.95)	(1.28*)	(1.23*)	(.58*)	(1.44*)	(.95)	(1.29*)	(1.03)	
Anxiety disorders												
PD	3	1	1	1	8	1	0	0	5	0	4	2
	(—)	(.50)	(.56)	(.22)	(5.78*)	(.61)	(—)	(—)	(2.74)	(—)	(2.12)	
PDA	11	11	11	4	20	10	11	23	22	14	21	12
	(.92)	(—)	(.91)	(.31*)	(1.82*)	(.85)	(.89)	(1.93)	(1.99*)	(1.19)	(1.86*)	
PD or PDA	14	12	13	5	27	12	11	23	27	14	25	14
	(1.00)	(.84)	(—)	(.30*)	(2.20*)	(.83)	(.76)	(1.67)	(2.13*)	(1.02)	(1.93*)	
SOC	8	19	18	1	39	27	16	15	43	52	45	21
	(.39)	(.87)	(.79)	(—)	(2.17*)	(1.36)	(.77)	(.74)	(2.32*)	(2.62*)	(2.54*)	
GAD	19	17	18	14	3	12	6	23	9	5	8	12
	(1.63)	(1.80*)	(1.93*)	(1.19)	(—)	(.96)	(.42*)	(1.92)	(.69)	(.39)	(.62)	
GAD: No hierarchy	22	23	23	22	3	16	7	38	67	90	72	23
	(.95)	(1.01)	(1.00)	(.91)	(—)	(.65)	(.29*)	(1.67)	(3.45*)	(4.15*)	(4.07*)	
OCD	8	10	10	10	8	4	4	31	14	5	12	9
	(.92)	(1.16)	(1.14)	(1.17)	(.92)	(—)	(.38)	(3.54*)	(1.58)	(.52)	(1.36)	
SPEC	14	18	18	10	17	13	20	23	19	10	17	16
	(.89)	(1.23)	(1.20)	(.59*)	(1.05)	(.80)	(1.23)	(1.46)	(1.18)	(.59)	(1.05)	
PTSD	3	8	8	4	7	1	2	0	10	0	8	5
	(.50)	(1.91*)	(1.75*)	(.64)	(1.26)	(.22)	(.31)	(—)	(1.95)	(—)	(1.51)	
Other anxiety	8	6	7	4	4	4	5	0	2	0	2	5
	(1.73)	(1.55)	(1.69)	(.84)	(.82)	(.77)	(1.11)	(—)	(.48)	(—)	(.37)	
Mood disorders												
MDD	36	52	50	44	64	61	27	77	52	76	57	50
	(.71)	(1.04)	(1.00)	(.87)	(1.33*)	(1.24*)	(.51*)	(1.55*)	(—)	(1.54*)	(—)	
DYS	11	9	4	17	13	12	7	23	12	5	11	11
	(.99)	(.69)	(.70)	(1.67*)	(1.13)	(1.04)	(.62)	(2.08)	(1.11)	(—)	(—)	
Other mood	6	6	6	11	9	10	6	8	1	5	2	7
	(.74)	(.82)	(.79)	(1.62)	(1.27)	(1.44)	(.84)	(1.03)	(.15)	(.64)	(.24*)	
Other disorders												
Alcohol	17	17	17	15	12	9	7	31	16	29	19	15
	(1.14)	(1.29)	(1.31)	(1.03)	(.77)	(.60)	(.47*)	(2.13)	(1.10)	(1.99)	(1.31)	
Drug	6	11	11	11	10	5	9	23	7	14	9	10
	(.55)	(1.17)	(1.09)	(1.16)	(1.00)	(.50)	(.90)	(2.34)	(.72)	(1.44)	(.87)	
Alcohol or drug	19	23	22	17	18	10	12	38	17	29	20	19
	(1.05)	(1.36*)	(1.35*)	(.94)	(.93)	(.54)	(.61)	(2.10*)	(.92)	(1.56)	(1.06)	
Somatoform	0	2	2	2	6	4	2	0	2	0	2	2
	(—)	(.82)	(.70)	(.60)	(2.91*)	(1.65)	(.71)	(—)	(1.00)	(—)	(.77)	
Other Axis I	11	6	7	5	8	10	11	0	10	0	8	8
	(1.48)	(.79)	(.86)	(.73)	(1.10)	(1.40)	(1.51)	(—)	(1.33)	(—)	(1.03)	

Note. *DSM–IV* = *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition (American Psychiatric Association, 1994); PD = panic disorder; PDA = panic disorder with agoraphobia; PD/A = PD or PDA; SOC = social phobia; GAD = generalized anxiety disorder; GAD: No hierarchy = GAD ignoring *DSM–IV* hierarchy rule with mood disorders; OCD = obsessive–compulsive disorder; SPEC = specific phobia; PTSD = posttraumatic stress disorder; MDD = major depressive disorder; DYS = dysthymia; MDD/DYS = MDD or DYS; Alcohol = alcohol abuse/dependence; Drug = other substance abuse/dependence. Dashes in parentheses indicate that the odds ratio is inapplicable. Percentages in the diagonal are prevalence of multiple episodes of the same disorder (e.g., 3% of patients with PD reported distinct past episode of PD).

[a] Overall frequency category was assigned as an additional diagnosis.

* Significantly increased or decreased risk of co-occurring disorder (95% confidence interval).

rates increased markedly when lifetime diagnoses were examined. Overall, 81% of patients with a current principal anxiety or mood disorder had at least one additional lifetime Axis I diagnosis. By far, the most common additional lifetime diagnosis was MDD (50%), followed by SOC (21%) and the substance use disorders (19%). The principal diagnostic categories differed significantly in the rates of lifetime Axis I comorbidity, $\chi^2(8, N = 968) = 54.12$, $p < .001$. The rate of lifetime comorbidity was significantly elevated in the principal diagnoses of PTSD (100%, OR = 1.24), DYS (100%, OR = 1.25), GAD (92%, OR = 1.16), and MDD (91%, OR = 1.15). A significantly lower rate of lifetime Axis I comorbidity was noted in SPEC (65%, OR = .78) and SOC (72%, OR = .86).

Similarly, the rate of lifetime comorbid anxiety disorders significantly differed across principal diagnostic groups, $\chi^2(8, N = 968) = 56.52, p < .001$. Additional lifetime anxiety disorders were significantly more common in principal MDD (73%, OR = 1.40) and GAD (71%, OR = 1.38) and significantly less common in SOC (37%, OR = .63).

Collapsing across mood disorder types, 59% of patients with a principal *DSM–IV* diagnosis of an anxiety or mood disorder had a lifetime history of comorbid depression; 60% of patients with principal anxiety disorders had lifetime mood disorders. The rates of lifetime mood disorders differed significantly across the seven principal anxiety disorders, $\chi^2(6, N = 866) = 45.73, p < .001$. The principal diagnoses associated with significantly greater risk of lifetime comorbid mood disorders were PTSD (85%, OR = 1.44), GAD (73%, OR = 1.28), DYS (76%, OR = 1.29), and OCD (71%, OR = 1.23). Whereas these same categories were associated with elevated rates of lifetime MDD, principal SOC was the only disorder related to increased risk of lifetime DYS (17%, OR = 1.67). Lifetime mood disorders were significantly less common in principal SPEC (36%, OR = .58).

In addition, the nine principal diagnostic groups significantly differed in their rates of past alcohol use disorders (when abuse and dependence diagnoses were collapsed), $\chi^2(8, N = 968) = 15.55, p < .05$, although this was a somewhat weak effect (Cramér's $V = .13$), and the only significant association noted was a decreased likelihood of these conditions in principal SPEC (7%, OR = .47). The groups did not differ in past prevalence of drug use disorders, $\chi^2(8, N = 968) = 7.15$, *ns*, or when alcohol and drug use disorders were collapsed, $\chi^2(8, N = 968) = 15.14, p < .06$. It is interesting that although PDA and SOC have often been implicated as having a heightened risk of alcohol use disorders (Kushner et al., 1990), the co-occurrences of these past conditions in these principal diagnoses (17% and 15%, respectively) were not significantly elevated relative to the sample base rate (15%). Note that the figures in Table 2 are underestimates of lifetime prevalence, given the sample selection criterion excluding patients with a recent (past 6 months) clinical episode of substance abuse or dependence.

Comorbidity in DSM–IV Anxiety and Mood Disorders Anywhere in the Clinical Picture

Current diagnoses. Table 3 presents percentages and ORs for current *DSM–IV* disorders, with principal and additional diagnoses collapsed. Three of the seven anxiety disorders, SOC, OCD, and PTSD, were associated with significantly elevated risk of MDD (32% to 65%, ORs = 1.29 to 2.51). The only anxiety disorders linked to heightened risk of DYS were SOC (17%, OR = 2.18) and PTSD (20%, OR = 1.91). PTSD and SOC had the highest comorbidity rates with depression, when the types of mood disorder were collapsed (80% and 48%, respectively). Indeed, PTSD and SOC were the only anxiety disorders associated with a higher prevalence of mood disorders of any type (ORs = 2.15 and 1.42, respectively).

Findings in Table 3 also reflect a significant association between PDA and PTSD. PTSD was the only anxiety or mood diagnosis associated with a significantly elevated risk of PDA (55%, OR = 1.51). Conversely, when PDA was present, the risk of PTSD was elevated twofold (OR = 2.06). These results also indicate particularly strong comorbidity between MDD and PTSD (10%)—PTSD was nearly 5 times more likely when MDD was present than when MDD was absent (OR = 4.92). In addition, both MDD and DYS were associated with significantly higher comorbidity rates of SOC (43%, OR = 1.24; and 56%, OR = 1.62, respectively) and GAD when *DSM–IV* hierarchy rules were ignored (57%, OR = 2.09; and 50%, OR = 1.47, respectively).

Lifetime diagnoses. Table 4 presents the comorbidity of lifetime diagnoses when principal and additional disorders were collapsed. The pattern of comorbidity among lifetime anxiety and mood disorders was similar to the covariation seen in current diagnoses. For example, as in current diagnoses, the presence of lifetime SOC, OCD and PTSD was associated with significantly higher prevalence of lifetime MDD (60% to 82%, ORs = 1.18–1.56); in addition, GAD evidenced a significant comorbidity rate with MDD (67%, OR = 1.29). Whereas these four anxiety disorders were also associated with elevated risk of lifetime mood disorders of any type (72%–91%; ORs = 1.23–1.49), SOC was the only anxiety disorder linked to increased prevalence of DYS (OR = 1.92).

Also consistent with the results using current diagnoses, lifetime PTSD was the only anxiety or mood disorder associated with elevated risk of PDA (60%, OR = 1.53), although it is noteworthy that PD was significantly more likely to be present given a lifetime diagnosis of GAD (9%, OR = 1.78; in addition, presence of PD predicted comorbid GAD: 37%, OR = 1.54). Although MDD was the strongest predictor of PTSD (11%, OR = 3.75), a lifetime diagnosis of PTSD was also significantly more likely to occur if there was a lifetime history of PDA (11%, OR = 2.18) and OCD (11%, OR = 1.64). The converse was also true in that the presence of PTSD was indicative of a significantly higher rate of comorbid OCD (24%, OR = 1.54).

In addition to PTSD, the presence of a lifetime diagnosis of MDD was associated with significantly higher risk of the anxiety disorders of SOC (44%, OR = 1.25), GAD (30%, OR = 1.60), and OCD (20%, OR = 1.70). Although the strongest predictor of lifetime SOC (56%, OR = 1.51), a lifetime history of DYS was not significantly related to increased risk of any other emotional disorder except MDD (64%, OR = 1.22).

Although somatoform disorders were diagnosed infrequently in the sample, the presence of lifetime GAD and MDD increased the risk of these conditions over twofold (4%, OR = 2.15; and 3%, OR = 2.20, respectively). As seen in Table 4, three lifetime disorders were associated with a significantly higher rate of past alcohol use disorders: PTSD (30%, OR = 2.21), MDD (20%, OR = 2.05), and PDA (18%, OR = 1.32). PTSD and MDD were

Table 3
Overall Percentage Rates (and Odds Ratios) of Co-Occurrence of Current Anxiety and Mood Disorders (N = 1,127)

Co-occurring diagnosis	Index *DSM–IV* diagnosis (*n*)											
	PD (51)	PDA (421)	PD/A (472)	SOC (416)	GAD (270)	OCD (156)	SPEC (250)	PTSD (49)	MDD (312)	DYS (125)	MDD/DYS (394)	Overall[a]
Any Axis I	59	71	69	75	86	79	71	98	92	96	92	100
Any anxiety/mood	59	70	68	75	83	77	70	98	91	95	92	100
Any anxiety disorder	53	56	56	59	77	67	66	88	89	89	90	96
Any mood disorder	37	41	40	48	40	46	34	80	14	35	11	39
Anxiety disorders												
PD	—	—	—	3	6	3	3	0	4	3	4	5
				(.53*)	(1.59)	(.53)	(.65)	(—)	(.99)	(.68)	(.85)	
PDA	—	—	—	23	34	26	30	55	41	31	39	37
				(.50*)	(.90)	(.67*)	(.75*)	(1.51*)	(1.15)	(.82)	(1.08)	
PD or PDA	—	—	—	26	41	29	33	55	46	34	43	42
				(.50*)	(.96)	(.66*)	(.74*)	(1.33*)	(1.14)	(.80)	(1.06)	
SOC	24	23	23	—	42	35	27	41	43	56	45	37
	(.63)	(.50*)	(.48*)		(1.18)	(.93)	(.69*)	(1.11)	(1.24*)	(1.62*)	(1.41*)	
GAD	33	22	23	27	—	22	20	22	25	14	23	24
	(1.42)	(.88)	(.95)	(1.23)		(.90)	(.80)	(.93)	(1.08)	(.54*)	(.95)	
GAD: No hierarchy	43	33	34	43	—	35	30	45	57	50	56	36
	(1.22)	(.88)	(.92)	(1.36*)		(.96)	(.79*)	(1.27)	(2.09*)	(1.47*)	(2.23*)	
OCD	8	10	10	13	13	—	11	22	18	14	16	14
	(.56)	(.60*)	(.56*)	(.90)	(.88)		(.73)	(1.67)	(1.42*)	(.98)	(1.34)	
SPEC	16	18	17	16	19	17	17	27	17	23	19	22
	(.70)	(.71*)	(.68*)	(.64*)	(.79)	(.75)	(—)	(1.21)	(.70*)	(1.05)	(.77*)	
PTSD	0	6	6	5	4	7	5	—	10	8	9	4
	(—)	(2.06*)	(1.70)	(1.18)	(.92)	(1.80)	(1.27)		(4.92*)	(2.06*)	(5.15*)	
Other anxiety	2	4	4	4	1	3	7	2	4	6	5	8
	(.23)	(.41*)	(.36*)	(.42*)	(.11*)	(.36*)	(.85)	(.24)	(.43*)	(.66)	(.48*)	
Mood disorders												
MDD	27	31	30	32	29	35	21	65	—	34	—	28
	(.99)	(1.18)	(1.17)	(1.29*)	(1.08)	(1.33*)	(.72*)	(2.51*)		(1.28)		
DYS	8	9	9	17	6	11	12	20	14	—	—	11
	(.70)	(.76)	(.73)	(2.18*)	(.50*)	(.98)	(1.06)	(1.91*)	(1.37)			
Other mood	6	4	4	5	6	4	5	6	0	1	0	4
	(1.51)	(.93)	(1.01)	(1.37)	(1.93*)	(.96)	(1.26)	(1.57)	(—)	(.18)	(.04*)	
Other disorders												
Somatoform	0	2	1	1	3	3	0	4	2	2	3	2
	(—)	(1.07)	(.88)	(.85)	(2.02)	(1.78)	(—)	(2.75)	(1.66)	(1.60)	(2.23)	
Other Axis I	6	5	6	5	7	7	5	6	8	6	8	6
	(1.07)	(.99)	(1.00)	(.88)	(1.51)	(1.34)	(.93)	(1.12)	(1.89*)	(1.19)	(1.74*)	

Note. *DSM–IV* = *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition (American Psychiatric Association, 1994); PD = panic disorder; PDA = panic disorder with agoraphobia; PD/A = PD or PDA; SOC = social phobia; GAD = generalized anxiety disorder; GAD: No hierarchy = GAD ignoring *DSM–IV* hierarchy rule with mood disorders; OCD = obsessive–compulsive disorder; SPEC = specific phobia; PTSD = posttraumatic stress disorder; MDD = major depressive disorder; DYS = dysthymia; MDD/DYS = MDD or DYS. Index diagnosis = when the category listed in the column is present, the risk of having the co-occurring disorder (listed in rows) is indicated by percentage and odds ratio. Dashes in parentheses indicate that the odds ratio is inapplicable.

[a] Overall frequency category was assigned as a current diagnosis in the sample.

* Significantly increased or decreased risk of co-occurring disorder (95% confidence interval).

also linked to increased risk of substance use disorders other than alcohol (18%, OR = 1.87; and 13%, OR = 2.05, respectively). When alcohol and drug use disorders were collapsed, these conditions were significantly more likely to occur if a lifetime diagnosis of PTSD, MDD, or PDA was present (23%–34%, ORs = 1.42–1.90).

Some current and lifetime disorders in Tables 3 and 4 were routinely associated with decreased risk of other conditions. This was particularly true for the phobic disorders (i.e., PDA, SOC, and SPEC). For example, the presence of current PDA was predictive of a lower risk of SOC and SPEC (ORs = .50 and .71). In addition, significantly lower associations between current DYS and GAD (ORs < .54) were noted, although this finding can be attributed to an artifact arising from the *DSM–IV* hierarchy rule for diagnosing GAD in the context of co-occurring mood disorders. However, in some cases, such findings may represent a true lack of covariation between disorders; for example, the presence of current SPEC was predictive of significant decreased risk of MDD (OR = .72), perhaps indicative of lower co-occurrence of mood disorders with this diagnosis.

Age of onset and temporal sequence of lifetime disorders. Table 5 presents average ages of onset and temporal sequences for lifetime diagnoses of the major anxiety and mood disorders and alcohol/substance use disorders. When multiple disorder episodes

Table 4
Overall Percentage Rates (and Odds Ratios) of the Co-Occurrence of Lifetime DSM–IV Anxiety and Mood Disorders (N = 1,127)

Co-occurring diagnosis	Index *DSM–IV* diagnosis (*n*)											
	PD (65)	PDA (456)	PD/A (512)	SOC (449)	GAD (279)	OCD (185)	SPEC (278)	PTSD (82)	MDD (613)	DYS (159)	MDD/DYS (670)	Overall[a]
Any Axis I	86	87	87	88	96	94	86	100	99	100	99	100
Any anxiety/mood	83	82	82	86	94	93	82	100	99	99	99	100
Any anxiety disorder	69	64	64	67	85	74	76	94	95	92	95	97
Any mood disorder	55	67	66	72	74	77	60	91	57	69	53	64
Anxiety disorders												
PD	2	2	0	4	9	3	4	1	5	6	5	6
	(—)	(.24*)	(—)	(.53*)	(1.78*)	(.52)	(.62)	(.20)	(.72)	(.98)	(.70)	
PDA	14	10	9	27	40	30	37	60	43	35	43	40
	(.33*)	(—)	(—)	(.55*)	(.97)	(.71*)	(.85)	(1.53*)	(1.12)	(.85)	(1.14)	
PD or PDA	15	12	11	30	47	33	39	60	47	40	47	45
	(—)	(—)	(—)	(.55*)	(1.05)	(.69*)	(.83*)	(1.35*)	(1.10)	(.87)	(1.10)	
SOC	26	27	27	0	46	38	34	43	44	56	45	40
	(.64*)	(.55*)	(.52*)	(—)	(1.20*)	(.94)	(.82*)	(1.08)	(1.25*)	(1.51*)	(1.43*)	
GAD	37	24	26	28	1[illegible]	24	22	30	30	20	29	25
	(1.54*)	(.96)	(1.06)	(1.26*)	(—)	(.98)	(.85)	(1.25)	(1.60*)	(.79)	(1.56*)	
GAD: No hierarchy	55	64	63	57	3	62	68	50	52	51	52	64
	(.86)	(1.02)	(.99)	(.83*)	(—)	(.97)	(1.08)	(.77*)	(.66*)	(.78*)	(.65*)	
OCD	9	12	12	16	16	3	14	24	20	14	20	16
	(.55)	(.64*)	(.59*)	(.92)	(.98)	(—)	(.82)	(1.54*)	(1.70*)	(.86)	(1.66*)	
SPEC	17	22	21	21	22	21	19	33	23	27	24	25
	(.67)	(.82)	(.77*)	(.78*)	(.85)	(.83)	(—)	(1.37)	(.89)	(1.11)	(.91)	
PTSD	2	11	10	8	9	11	10	4	11	9	11	7
	(.20)	(2.18*)	(1.78*)	(1.12)	(1.33)	(1.64*)	(1.50)	(—)	(3.75*)	(1.36)	(4.91*)	
Other anxiety	8	6	6	7	4	5	9	2	7	10	7	10
	(.77)	(.50*)	(.49*)	(.56*)	(.30*)	(.45*)	(.89)	(.23)	(.53*)	(1.03)	(.52*)	
Mood disorders												
MDD	46	57	57	60	67	67	51	82	28	64	26	54
	(.84)	(1.09)	(1.08)	(1.18*)	(1.29*)	(1.29*)	(.93)	(1.56*)	(—)	(1.22*)	(—)	
DYS	14	12	13	20	11	12	15	18	17	3	1	14
	(.98)	(.80)	(.81)	(1.92*)	(.77)	(.86)	(1.13)	(1.33)	(1.50*)	(—)	(—)	
Other mood	8	6	7	8	10	9	8	11	5	4	5	7
	(1.05)	(.79)	(.83)	(1.21)	(1.63*)	(1.31)	(1.03)	(1.55)	(.50*)	(.56)	(.52*)	
Other disorders												
Alcohol	14	18	17	17	16	12	14	30	20	17	19	15
	(.92)	(1.32*)	(1.34*)	(1.26)	(1.14)	(.80)	(.95)	(2.21*)	(2.05*)	(1.16)	(2.06*)	
Drug	8	12	11	11	11	9	10	18	13	11	12	10
	(.73)	(1.22)	(1.18)	(1.13)	(1.14)	(.87)	(.96)	(1.87*)	(1.61*)	(1.03)	(1.53*)	
Alcohol or drug	18	23	23	21	22	16	19	34	24	21	23	19
	(.96)	(1.39*)	(1.42*)	(1.19)	(1.17)	(.79)	(.99)	(1.90*)	(1.71*)	(1.14)	(1.69*)	
Somatoform	0	3	3	3	4	3	1	4	3	4	4	3
	(—)	(1.58)	(1.29)	(1.23)	(2.15*)	(1.33)	(.49)	(1.47)	(2.20*)	(1.94)	(3.27*)	
Other Axis I	9	6	6	8	7	10	12	12	7	9	7	8
	(1.15)	(.69)	(.68)	(.90)	(.86)	(1.34)	(1.66*)	(1.57)	(.82)	(1.11)	(.80)	

Note. *DSM–IV* = *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition (American Psychiatric Association, 1994); PD = panic disorder; PDA = panic disorder with agoraphobia; PD/A = PD or PDA; SOC = social phobia; GAD = generalized anxiety disorder; GAD: No hierarchy = GAD ignoring *DSM–IV* hierarchy rule with mood disorders; OCD = obsessive–compulsive disorder; SPEC = specific phobia; PTSD = posttraumatic stress disorder; MDD = major depressive disorder; DYS = dysthymia; MDD/DYS = MDD or DYS; Alcohol = alcohol abuse/dependence; Drug = other substance abuse/dependence. Percentages in the diagonal are prevalence of multiple episodes of the same disorder (e.g., 2% of patients with PD reported >1 distinct episode of PD). Index diagnosis = when the category listed in the column is present, the risk of having the co-occurring disorder (listed in rows) is indicated by percentage and odds ratio. Dashes in parentheses indicate that the odds ratio is inapplicable.

[a] Overall frequency category was assigned as a lifetime diagnosis.

* Significantly increased or decreased risk of co-occurring disorder (95% confidence interval).

were evident (e.g., recurrent MDD), age of onset was defined by the first occurrence of the disorder. In addition to calculation of mean differences in the ages of onset of comorbid disorders, the relative age of onset of disorders was categorized as *temporally primary* (onset of comorbid disorder occurred over 1 year before index disorder), *same year* (both disorders had ages of onset within 12 months), and *temporally secondary* (onset of comorbid disorder occurred over 1 year after index disorder), following methods used in epidemiological studies (e.g., Kessler et al., 1997, 1998; Magee et al., 1996).

It is clear that SOC was associated with the earliest age of onset (M = 15.70 years) and was the disorder that most often preceded other conditions (e.g., the frequency with which other anxiety disorders or mood disorders occurred before SOC was 32% and

Table 5
Age of Onset and Temporal Sequence of Lifetime DSM–IV Anxiety, Mood, and Substance Use Disorders (N = 1,089)

	Index *DSM–IV* diagnosis (*n*)[a]									
	SOC (433)	DRUG (115)	DYS (152)	SPEC (269)	GAD (273)	ALC (161)	PTSD (81)	OCD (169)	PD/A (492)	MDD (592)
Age of Onset:										
M	15.70	18.96	19.33	20.29	20.57	21.08	21.54	22.03	25.99	26.36
(*SD*)	(9.42)	(5.22)	(11.36)	(13.23)	(11.50)	(6.52)	(10.89)	(10.29)	(9.74)	(10.53)
	Age of onset difference with comorbid diagnosis									
DRUG (*n*)	45									
M (*SD*)	3.24 (9.70)									
Prim/same/sec (%)	33/02/64									
DYS (*n*)	81	21								
M (*SD*)	2.96 (13.07)	1.54 (10.67)								
Prim/same/sec (%)	20/26/54	48/5/48								
SPEC (*n*)	93	23	41							
M (*SD*)	4.03 (12.47)	−4.58 (10.09)	−4.48 (13.63)							
Prim/same/sec (%)	37/10/54	70/4/26	54/12/34							
GAD (*n*)	125	33	32	60						
M (*SD*)	2.90 (10.78)	−1.88 (13.54)	−3.03 (18.18)	−0.24 (12.53)						
Prim/same/sec (%)	25/25/50	45/6/48	53/16/31	43/7/50						
ALC (*n*)	73	67	25	37	44					
M (*SD*)	7.76 (8.79)	0.18 (5.63)	1.52 (13.95)	0.60 (13.32)	4.97 (11.27)					
Prim/same/sec (%)	14/10/77	27/37/36	36/4/60	46/5/49	34/2/64					
PTSD (*n*)	33	13	14	27	26	25				
M (*SD*)	6.76 (12.07)	−0.81 (8.17)	4.14 (10.86)	2.47 (12.96)	7.58 (12.85)	−1.35 (12.18)				
Prim/same/sec (%)	30/12/58	62/0/38	29/21/50	30/11/59	31/4/65	64/4/32				
OCD (*n*)	60	15	19	37	42	23	20			
M (*SD*)	7.27 (10.71)	3.76 (12.39)	7.72 (15.53)	5.46 (13.78)	5.72 (12.70)	1.53 (9.82)	1.23 (13.77)			
Prim/same/sec (%)	27/5/68	20/7/73	32/16/53	27/8/65	26/17/57	43/13/43	45/5/50			
PD/A (*n*)	129	57	62	104	126	84	47	58		
M (*SD*)	11.28 (12.45)	5.33 (7.59)	6.04 (12.18)	8.77 (12.12)	5.43 (11.60)	5.59 (9.37)	3.41 (9.91)	1.25 (10.21)		
Prim/same/sec (%)	10/12/78	18/7/75	19/8/73	13/16/70	21/23/56	21/12/67	28/17/55	29/28/43		
MDD (*n*)	257	71	100	139	178	113	65	112	278	
M (*SD*)	10.29 (12.22)	4.65 (9.60)	10.64 (13.50)	10.45 (14.44)	7.21 (11.37)	4.46 (10.23)	2.34 (9.45)	3.24 (10.07)	0.63 (9.50)	
Prim/same/sec (%)	12/12/76	23/7/69	14/4/82	21/6/73	18/16/66	27/13/60	28/29/43	28/19/54	32/31/37	
Any Anxiety (*n*)	270	107	139	182	229	153	76	123	296	550
M (*SD*)	3.50 (11.54)	−2.51 (10.24)	−3.27 (13.33)	−0.74 (13.56)	−1.55 (11.36)	−5.12 (9.76)	−6.05 (12.47)	−6.55 (11.83)	−8.64 (12.53)	−8.82 (11.82)
Prim/same/sec (%)	32/16/51	52/5/43	56/20/24	43/11/46	49/23/28	64/10/26	58/11/32	63/11/26	70/15/15	69/18/13
MDD or DYS (*n*)	288	78		154	189	119	69	117	303	
M (*SD*)	7.24 (12.09)	2.36 (9.34)		7.06 (13.68)	5.71 (12.07)	2.42 (10.68)	0.44 (9.90)	1.07 (11.19)	−1.36 (9.86)	
Prim/same/sec (%)	15/17/68	35/6/59		28/8/64	22/16/62	34/13/53	35/29/36	32/19/49	43/26/31	

Note. Index *DSM–IV* disorders are listed in chronological order of their mean ages of onset. *DSM–IV = Diagnostic and Statistical Manual of Mental Disorders,* 4th edition (American Psychiatric Association, 1994); PD/A = panic disorder with or without agoraphobia; SOC = social phobia; GAD = generalized anxiety disorder; OCD = obsessive–compulsive disorder; SPEC = specific phobia; PTSD = posttraumatic stress disorder; MDD = major depressive disorder; DYS = dysthymia; ALC = alcohol abuse/dependence; DRUG = other substance abuse/dependence; Any anxiety = PD/A, SOC, GAD, OCD, SPEC, or PTSD; Prim/Same/Sec = primary/same year/secondary (i.e., percentage of cases in which onset of comorbid disorder occurred prior to index disorder; percentage of cases in which onset of comorbid disorder occurred within the same year as index disorder; and percentage of cases in which onset of comorbid disorder occurred after index disorder). Example: Of the 45 patients with lifetime SOC and DRUG comorbidity, on average, the age of onset of DRUG was 3.24 years after SOC onset (*SD* = 9.70 years); in 64% of these patients, the onset of DRUG was temporally secondary to the onset of SOC.

[a] Frequency of index diagnosis in the *N* = 1,089 sample (1,127 minus 38 cases where age of onset data were missing).

15%, respectively). In addition to frequently preceding MDD and DYS (66% and 53%, respectively), GAD tended to be temporally primary to other anxiety disorders (range = 56–65%), except SOC (25%) and SPEC (43%). Consistent with epidemiological findings (Magee et al., 1996), panic disorder with or without agoraphobia (PD/A) had the oldest age of onset (M = 25.99 years) of the anxiety disorders and was typically a secondary disorder (another anxiety disorder preceded PD/A in 70% of cases).

Although MDD infrequently occurred prior to anxiety disorders (range = 12%–32%), DYS was often temporally primary to PTSD (50%), OCD (53%), and PD/A (73%). As with MDD, DYS preceded SOC, SPEC, and GAD relatively infrequently (20%, 34%, and 31%, respectively). Similarly, considerable variability in temporal sequence was noted among the substance use disorders and anxiety and mood disorders. For instance, in the aggregate, anxiety disorders preceded alcohol abuse/dependence in 64% of comorbid cases; yet, this temporal sequence was strongest for SOC (77%), PTSD (64%), and GAD (64%). In contrast, alcohol use disorders were temporally primary in 43% and 46% of cases involving comorbid OCD and SPEC, respectively. The primacy of alcohol use disorders was particularly strong for PD/A and MDD—these disorders preceded PD/A and MDD in 67% and 60% of comorbid cases, respectively.

Discussion

Current and Lifetime Comorbidity Among DSM–IV Anxiety and Mood Disorders

Overall comorbidity. Consistent with findings based on prior *DSM* editions, these results underscore the fact that the *DSM–IV* anxiety and mood disorders rarely occur in isolation from other current or past Axis I conditions. Of the 968 patients with current principal anxiety or mood diagnoses, current and lifetime comorbidity with other Axis I disorders was 57% and 81%, respectively; current and lifetime comorbidity with other anxiety or mood disorders was 55% and 76%, respectively (Tables 1 and 2). In general, comorbidity was even higher for most diagnoses in analyses that collapsed across principal, additional, and lifetime disorders (Tables 3 and 4).

These findings are particularly striking in view of the possibility that aspects of the study methods resulted in underestimates of patient comorbidity. Factors that may have contributed to underestimation include (a) use of an assessment instrument that did not evaluate the entire range of Axis I and II conditions, and (b) study entry criteria that excluded patients with severe emotional disorders (e.g., active suicidal ideation) and certain comorbid patterns (e.g., current substance use disorders). Moreover, the observed rates and patterns of comorbidity should be interpreted cautiously in light of sampling issues such as probable self-selection biases leading to an underrepresentation of PTSD, certain mood disorders (e.g., bipolar disorder), and lowered rates of MDD and DYS as principal diagnoses (e.g., although MDD was the most common lifetime diagnosis in the sample, n = 613, it was the fifth most common principal diagnosis, n = 81). Although our Center's referral sources were informed that PTSD and mood disorders have the same admission priority and treatment eligibility as anxiety disorders, the low sample sizes associated with these categories (e.g., PTSD and DYS as principal diagnoses) indicate that self-selection and referral biases were operative and resulted in disproportionately lower sampling rates of these diagnoses relative to categories such as PD/A, SOC, and GAD. (For example, it is likely that patients with primary complaints of PTSD symptoms sought or were referred to specialty clinics offering services specific to their form of trauma).

As expected, substantial heterogeneity was found across *DSM–IV* diagnoses in the rates of overall current and lifetime comorbidity. Diagnoses with the highest overall comorbidity were PTSD, MDD, DYS, and GAD. Comorbidity rates of current additional Axis I disorders were lower in principal SPEC, PD, and SOC but were nonetheless quite marked when lifetime diagnoses were considered (65%, 75%, and 72% for SPEC, PD, and SOC, respectively; Table 2). These findings emphasize the importance of lifetime comorbidity in the evaluation of associated conditions and impairment in persons with anxiety or mood disorders. As another example, in analyses of current diagnoses, principal PD and PDA differed substantially in their rates of Axis I comorbidity (42% and 62%, respectively; Table 1), suggesting that the presence of agoraphobia is associated with higher comorbidity in patients with panic disorder. However, differences in comorbidity rates were negligible when lifetime disorders were considered (75% and 82% for PD and PDA, respectively; Table 2) and when lifetime disorders were analyzed ignoring principal diagnostic status (86% and 87% for PD and PDA, respectively; Table 4). Such findings suggest a cross-sectional relationship between agoraphobia and comorbidity that does not generalize to, or characterize differences in, the lifetime psychological disorder histories of patients with PD and PDA.

Although findings in Tables 3 and 4 are most comparable to results of epidemiological studies (i.e., analysis of comorbidity ignoring the relative severity of disorders; e.g., Kessler et al., 1998), the additional data in Tables 1 and 2, which present current and lifetime comorbidity by principal diagnoses, collectively provide a more comprehensive examination of the comorbidity issue. Findings in Table 1 are likely to be most germane to practicing clinicians interested in rates and patterns of comorbidity associated with the disorder representing the presenting complaint, and to scientists involved in treatment outcome and psychopathology research, in which the common scientific practice entails selection criteria for the currently most interfering/distressing condition. For example, it would be somewhat erroneous for the investigator designing a treatment outcome study for SPEC to anticipate, on the basis of findings in Table 3, that nearly three quarters (71%) of recruited patients will have Axis I comorbidity. Rather, the finding that 34% of patients with principal SPEC had additional Axis I disorders (Table 1) is more relevant to this researcher and indicates that a considerable degree of the SPEC comorbidity shown in Table 3 involved cases where SPEC was a relatively less severe condition that co-occurred with other more debilitating disorders. Moreover, although the overall covariation of disorders (Tables 3 and 4) is typically of greatest interest to comorbidity researchers, consideration of comorbidity as a function of principal diagnoses (Tables 1 and 2) frequently provides important clarification and information to this endeavor. For instance, the statistically significant covariation shown in Table 4 between lifetime PTSD and OCD is attributable primarily to cases in which PTSD is more severe than OCD and cases in which the PTSD precedes the OCD (see Table 5). In Table 1, note that principal PTSD is associated

with a 3.62 times greater risk of OCD; conversely, none of the cases of principal OCD had co-occurring PTSD. Collectively, these findings have greater heuristic value than findings that simply depict a marked lifetime aggregation of these disorders (e.g., indicate the possibility that the precipitants or features of PTSD act as etiological factors in comorbid OCD).

However, findings of comorbidity as a function of principal disorders should be interpreted while keeping in mind the potential difficulties (e.g., measurement error) associated with the distinction between principal and additional diagnoses. On one hand, results of T. A. Brown et al. (2001) suggest that the designation of principal diagnoses can be made with favorable levels of interrater agreement (κs for principal diagnoses ranged from .67 to .86, except DYS κ = .22). Note that, in addition to the use of the test–retest method (2 independent *ADIS–IV–L*s), reliability estimates for principal diagnoses in T. A. Brown et al. (2001) were established in a relatively stringent manner (i.e., even when both interviewers agreed on the presence of a given disorder, a case was counted as a disagreement when the interviewers did not concur on its *principal* vs. *additional* diagnostic status). Although this is encouraging, other considerations and evidence indicate that the determination of principal diagnoses is not straightforward. Although our operational definition of "principal diagnosis" (see Method) aligns closely with (but is not identical to) *DSM–IV* convention and terminology (American Psychiatric Association, 1994, p. 3), in some minority of cases the disorder judged by the interviewer to be the principal diagnosis differed from the disorder reported by the patient as their presenting complaint (moreover, in rare instances, patients' self-appraisals of their primary psychological difficulty varied within or between interviews). In addition to the fact that the distinction of principal versus additional diagnoses was not 100% reliable in T. A. Brown et al. (2001), further evidence of the difficulty in making these determinations is the finding that 9% of the current sample was assigned coprincipal disorders (see Footnote 3). Thus, although specification of principal disorders can provide a richer analysis of comorbidity and other issues in psychopathology, the operational guidelines and implementation of this designation are not straightforward and free of error.

Comparison to DSM–III–R estimates. Several noteworthy similarities and differences were evident in comparisons of current comorbidity rates with principal *DSM–IV* disorders with estimates from our *DSM–III–R* study (T. A. Brown, 1996; T. A. Brown & Barlow, 1992). For instance, the rate of current anxiety/mood disorder comorbidity (55%) is similar, albeit slightly higher, than the estimate obtained in our study of principal *DSM–III–R* anxiety and mood disorders (50%; T. A. Brown & Barlow, 1992; cf. T. A. Brown, 1996). Whereas *DSM–III–R* GAD had an overall comorbidity rate of 82% (similar results were obtained in Brawman-Mintzer et al., 1993, and Massion et al., 1993), in the present study only 68% of patients with principal GAD had additional Axis I disorders at the time of assessment. Nevertheless, the pattern of comorbidity associated with principal GAD was consistent across studies (e.g., mood disorders and SOC were the most common additional diagnoses, and OCD occurred infrequently; cf. Table 2 of T. A. Brown & Barlow, 1992; T. A. Brown et al., 1993). In fact, the overall comorbidity rate of GAD did not differ substantially from several other disorders (PTSD, MDD, DYS, and PDA). Although there are many potential explanations for this result (e.g., substantial revisions to the definition of *DSM–IV* GAD), this finding is particularly noteworthy, given that the high comorbidity rates previously found in GAD were used in strong support of the position to remove GAD as a formal diagnostic category in *DSM–IV* (T. A. Brown et al., 1994). Although these findings suggest that GAD may not be associated with undue comorbidity relative to several disorders, other results do indicate considerable overlap between GAD and other emotional disorders. For example, 92% of patients with principal GAD had other lifetime Axis I disorders (Table 2); if the *DSM–IV* hierarchy rule for mood disorders had been lifted, 90% of the patients with principal DYS would have been assigned current GAD (Table 1). However, only 5% of patients with principal DYS were assigned additional GAD when adhering to this hierarchy rule.

The principal diagnosis of SPEC had a 14% higher cross-sectional prevalence of Axis I comorbidity (34%; Table 1) compared with our *DSM–III–R* study (20%; cf. Figure 2.1 in T. A. Brown, 1996). The high comorbidity estimate for SPEC may have been due in part to a preponderance of situational type phobias in the sample (65 of the 110 patients with principal SPEC had situational phobias). Indeed, it has been suggested that situational phobias (e.g., driving, or enclosed places) are a more severe form of specific fears compared with the other, often more circumscribed phobia types (e.g., animals, or blood/injections; Antony, Brown, & Barlow, 1997). Besides GAD and SPEC, the overall cross-sectional comorbidity rates for principal *DSM–IV* anxiety and mood disorders were quite similar to rates in our *DSM–III–R* study (e.g., 46% vs. 45% for *DSM–IV* and *DSM–III–R* SOC, respectively; 57% vs. 56% for *DSM–IV* and *DSM–III–R* OCD, respectively; cf. Figure 2.1 in T. A. Brown, 1996).

Comorbidity Between DSM–IV Anxiety and Mood Disorders

Current and lifetime comorbid mood disorders were quite prevalent in the sample. The principal *DSM–IV* anxiety disorders associated with the highest mood disorder comorbidity were PTSD, GAD, and OCD (77%, 36%, and 32%, respectively, for current diagnoses; 85%, 73%, and 71%, respectively, for lifetime diagnoses). Nonetheless, in lifetime analyses, DYS was associated with increased risk of MDD indicating high overlap and possible poor discriminant validity of these disorders (cf. T. A. Brown et al., 2001). Although much evidence and conceptualization has pointed to the possible boundary problems between GAD and mood disorders, one could argue that these diagnostic comorbidity data do not uphold this position given the high mood disorder comorbidity obtained for disorders such as PTSD, OCD, SOC, and PDA. However, note that the degree of comorbidity between GAD and mood disorders is strongly influenced by the *DSM–IV* definitional criteria of these diagnoses; namely, GAD should not be assigned when it occurs during the course of a mood disorder (or PTSD). When this criterion was ignored, a substantially different picture emerged regarding the cross-sectional comorbidity of GAD and mood disorders. For instance, unlike the rates of additional GAD when *DSM–IV* criteria were strictly followed (5% for both MDD and DYS), the rates of comorbid GAD rose sharply to 67% and 90% for principal MDD and DYS, respectively, when the hierarchy rule was ignored (Table 1). These rates were much higher than those obtained for other principal diagnoses (the next

highest was 38% for PTSD). In addition to illustrating a limitation of diagnostic comorbidity data in the validation of the *DSM* nosology (e.g., degree of diagnostic co-occurrence can be an artifact of definitional criteria of disorders), these findings support evidence from other sources regarding the differential relationship of GAD and depression relative to other anxiety disorders (e.g., in T. A. Brown et al., 1998: Although latent structure analyses indicated that GAD dimensional features were factorially distinct from the features of mood disorders, these factors were highly correlated, $r = .63$, in comparison to zero-order intercorrelations among other *DSM–IV* disorder latent factors, range = .22–.50.).

PTSD and OCD were frequently accompanied by current or lifetime mood disorders, in support of prior evidence of the associations of these conditions with the affective disorders (e.g., Antony, Downie, & Swinson, 1998; Breslau, Davis, Peterson, & Schultz, 1997; Douglass, Moffitt, Dar, McGee, & Silva, 1995). However, of particular interest were findings indicating a significant aggregation of the mood disorders and SOC. For instance, by far the most frequent additional current or lifetime diagnosis in principal MDD and DYS was SOC (excluding other mood disorder diagnoses). These associations were confirmed by analyses collapsing across principal and additional diagnostic status. For both current and lifetime diagnoses, the presence of SOC was associated with a significantly increased risk of MDD and DYS, and vice versa. In fact, SOC was the only anxiety disorder to be associated with increased risk of both current and lifetime DYS (PTSD predicted risk of current DYS only). Indeed, for current disorders (Table 3), SOC had the second highest co-occurrence rate (48%) to the mood disorders. These results could be interpreted in accord with recent evidence that SOC and the mood disorders share specific features, and perhaps diatheses, not associated with other anxiety disorders (i.e., low positive affect; T. A. Brown et al., 1998; Clark et al., 1994; Watson, Clark, & Carey, 1988). For instance, T. A. Brown et al. (1998) found that the higher-order factor of Positive Affect had significant paths to the latent factors of *DSM–IV* Mood Disorders and Social Phobia but did not account for significant unique variance in latent factors corresponding to other *DSM–IV* anxiety disorders (PD/A, OCD, and GAD).

In addition, the present findings strongly support prior evidence of the relative infrequency of cases of "pure" depression (i.e., patients who present with mood disorders without current or past anxiety disorders; cf. Alloy, Kelly, Mineka, & Clements, 1990; Mineka et al., 1998). Of the 670 patients who had lifetime MDD or DYS (see Table 4), only 33 (5%) never had a current or past anxiety disorder. Although this quite low rate of pure depression could be partly due to sample bias (i.e., the research setting is better recognized as an "anxiety clinic" than a "mood disorders clinic," although no differential emphasis is placed on the recruitment or selection of anxiety and mood disorders), these results lend additional support to the empirical evidence and conceptualization of the shared diatheses of anxiety and mood disorders and the temporal sequence of these conditions (i.e., although anxiety and mood disorders share genetic and psychosocial vulnerability factors, anxiety disorders are often precursors to mood disorders; e.g., Alloy et al., 1990; Barlow, in press; T. A. Brown et al., 1998; Kendler et al., 1992; Mineka et al., 1998).

Differential Associations of Other DSM–IV Anxiety and Mood Disorders

The comorbidity associated with PTSD was strikingly high. The highest comorbidity rates were routinely found for PTSD, and lifetime PTSD was associated with significantly elevated risk of PDA, OCD, MDD, and substance use disorders (Table 4). ORs revealed a particularly strong link between PTSD and PDA—PTSD was the only lifetime diagnosis related to increased risk of PDA. Although speculative, this association may reflect the high level of autonomic arousability shared by these disorders. Unlike other anxiety and mood disorders, PTSD and PDA are characterized by high chronic autonomic arousal.[5] The high rate of lifetime PDA in PTSD (60%; Table 4) may uphold a theoretical account for comorbidity stating that the features of an existing disorder act as vulnerability for subsequent conditions (e.g., the chronicity of autonomic symptoms triggered by intrusive recollections of traumatic events in PTSD may develop into a clinical PD/A if fear of these somatic symptoms is present). Indeed, temporal sequence analyses indicated that in 72% of comorbid cases, PD/A followed or emerged within the same year as the onset of PTSD. The merit of such interpretation must be determined by a more fine-grained empirical analysis of this issue.

As noted earlier, findings regarding the past prevalence of substance use disorders are limited by the sample selection criteria, which excluded individuals meeting the *DSM–IV* threshold for these conditions in the 6 months preceding the evaluation. However, presuming that this exclusion criterion did not have a differential impact across the anxiety and mood disorders, results indicated that lifetime PTSD, MDD, and PDA were associated with significantly increased risk for alcohol use disorders and for substance use disorders of any kind (Table 4). It is plausible that the high levels of autonomic arousability associated with PTSD and PDA account in part for the higher likelihood of substance use disorders (i.e., greater motivation to "self-medicate" aversive symptoms of arousal; cf. Hull, 1981; Kushner et al., 1990; Sher, 1987). Whereas alcohol use disorders were indeed secondary to PTSD in 64% of comorbid cases, the converse was found for the temporal sequence involving PD/A—in 67% of cases, PD/A was preceded by alcohol abuse or dependence (Table 5). Although potentially due to an artifact of study exclusion criteria (i.e., comorbid cases of current PD/A and alcohol use disorders were excluded), this result may be reflective of the typical ages of onset of PD/A and alcohol use disorders. Unlike many anxiety disorders that usually begin before age 18 (e.g., SOC), epidemiological studies indicate that the average age of onset of PD/A is in the late 20s, near the end of the age range for the greatest incidence of alcohol disorders (Helzer, 1987).

Results also indicated that, for both current and lifetime disorders, the presence of some diagnoses (e.g., PDA) were routinely related to decreased risk of other conditions (e.g., SOC and SPEC). Instead of representing a true lack of association between these conditions (indeed, one would expect SOC and PDA to share many features, such as situational avoidance and fear of negative social

[5] Although panic attacks can occur in SOC and SPEC, these autonomic symptoms are usually confined to confrontations with phobic stimuli. Compare T. A. Brown et al. (1998), who found that PD/A was the only latent *DSM–IV* disorder factor to have a significant positive association with the latent factor of Autonomic Arousal.

evaluation when appearing anxious), these findings could be due to an artifact arising from *DSM–IV* differential diagnostic guidelines (i.e., symptoms of social or specific fear and avoidance were judged to be better accounted for and thereby subsumed under a PDA diagnosis). As we raised in the discussion of the unduly low co-occurrence of GAD and mood disorders owing to *DSM–IV* diagnostic hierarchy rules, these findings highlight the need for caution in the use of diagnostic comorbidity data in the evaluation of the *DSM* nosology as well as in the understanding of the nature, course, and complications of emotional disorders (cf. T. A. Brown, 1996, in press).

Temporal Sequence of Lifetime DSM–IV Anxiety and Mood Disorders

Consistent with previous findings (see Mineka et al., 1998, for a review), anxiety disorders were, in general, more likely to precede the onset of mood disorders. However, this temporal sequence was more evident for MDD than for DYS. In fact, for some anxiety disorders (PTSD, OCD, and PD/A), DYS was more often primary than secondary. The differing findings for MDD and DYS highlight the importance of analyzing these conditions separately rather than only analyzing a broad "mood disorders" category, a practice often seen in epidemiological research (cf. Magee et al., 1996). In accord with its characterological description (Klein, 1995), DYS had one of the earliest average ages of onset (M = 19.33 years) and was temporally primary to several co-occurring disorders. On the other hand, MDD had the latest age of onset (M = 26.36 years) and was usually secondary to other conditions. Although some evidence has led to concerns about the discriminant validity of DYS (e.g., low diagnostic reliability of DYS, often due to boundary issues with MDD; T. A. Brown et al., 2001), these data underscore a potentially important area of distinction between MDD and DYS. The fact that DYS often precedes anxiety disorders also has salient implications for etiological models of emotional disorders whose tenets are based partly on the temporal progression of anxiety to depression (e.g., the helplessness–hopelessness model; Alloy et al., 1990).

In comorbid cases, GAD most frequently predated DYS and MDD (53% and 66%, respectively). Given evidence of the shared genetic basis of GAD and mood disorders (e.g., Kendler et al., 1992), these data suggest that this vulnerability is often manifested by symptoms of GAD that progress to mood disorders in the context of the requisite environmental determinants (i.e., MDD represents "endstate" GAD; cf. Alloy et al., 1990; Barlow, in press). Addressing the possible poor discriminant validity of GAD, researchers have raised the notion that GAD might be better construed as a "prodrome" to mood disorders rather than a distinct Axis I entity. However, it is noteworthy that, on average, the onset of GAD predated the onset of MDD by 7.21 years (Table 5). Although undoubtedly affected to some degree by an artifact of adhering to *DSM–IV* diagnostic rules (e.g., GAD would not be diagnosed in cases in which these symptoms developed at the same time as mood disorders), these findings could be interpreted as being inconsistent with the "GAD as prodrome" position, given that many patients had an onset of MDD several years after GAD.

Whereas GAD was often primary to the anxiety disorders PD/A, OCD, and PTSD, this was not the case for SOC (and SPEC), in which GAD was temporally secondary in 50% of comorbid cases (e.g., on average, GAD followed the onset of SOC by 2.90 years). Because the key features of GAD correspond to those implicated as predispositional traits of the anxiety and mood disorders (i.e., negative affect and worry; Clark et al., 1994), some researchers have suggested that the high comorbidity rate associated with GAD may be due, in part, to its constituent symptoms acting as risk factors for co-occurring disorders (T. A. Brown et al., 1994). Although GAD–SOC comorbidity was high (e.g., 46% of patients with lifetime GAD had comorbid SOC), such an explanation may not be plausible given the relative infrequency with which GAD preceded SOC. However, note that the age of onset of disorders was defined by the time when symptoms met the *DSM–IV* diagnostic threshold, not by the initial emergence of disorder features (e.g., age of onset of PDA may not correspond to the time of the first uncued panic attack because this symptom alone does not satisfy *DSM–IV* criteria for PDA). Accordingly, findings of diagnostic temporal sequence do not necessarily refute or support this or other conceptual accounts of comorbidity because of the possible presence of subthreshold symptoms that influence the emergence and course of subsequent disorders (e.g., in many patients, subclinical levels of negative affect and worry may exist with etiological salience to SOC and other conditions). In many cases, clinically significant levels of early onset GAD may have been present but not recognized as a lifetime *DSM–IV* diagnosis because of adherence to differential diagnosis and diagnostic hierarchy rules in the nomenclature or because of measurement error in applying categorical cutoffs to inherently dimensional phenomena (i.e., the *DSM* threshold for presence/absence of a disorder; T. A. Brown et al., 2001). These considerations highlight the limitations of descriptive diagnostic comorbidity data in addressing theoretical issues regarding the classification, etiology, and nature of disorders (T. A. Brown & Barlow, in press; Widiger & Sankis, 2000).

Summary

The present study presents *DSM–IV* diagnostic comorbidity findings in a carefully diagnosed, large outpatient sample of persons with anxiety and mood disorders. Whereas current and lifetime comorbidity was high overall, particularly strong aggregations were noted for several comorbid patterns (e.g., SOC and mood disorders; PD/A and PTSD; and PTSD and mood disorders). In addition to their clinical utility (e.g., information for clinicians on the disorders most likely to co-occur with a presenting condition), these data have far-ranging implications for clinical research endeavors (e.g., in view of the high PTSD–mood disorder comorbidity, findings underscore the importance in clinical trials of not excluding comorbid cases and of evaluating the impact of this variable on treatment outcome).[6] Though typically associated with the topic of nosology, the contributions of diagnostic comorbidity data to this area are limited by the multitude of potential explanations for descriptive findings and problems associated with use of categorical, *DSM–IV*-defined diagnoses (e.g., unduly low associations between GAD and mood disorders, or between PDA and phobic disorders, when *DSM–IV* diagnostic rules are followed

[6] Indeed, exclusion of comorbid MDD is a common practice in treatment outcome studies of anxiety disorders despite substantial compromises to external validity and the neglected opportunity to evaluate a potentially powerful predictor of treatment success (T. A. Brown & Barlow, 1992).

strictly). Although descriptive comorbidity findings have considerable heuristic value, most important questions on the classification of emotional disorders would be optimally addressed by methodologies involving dimensional indicators of the shared and unique features of disorders and their vulnerabilities (cf. T. A. Brown et al., 1998). Such an approach allows for a more compelling evaluation of the cross-sectional and temporal covariation of psychopathological features, free from many possible biases of the current nosology and from error and information loss resulting from imposition of a categorical threshold on the expression of symptom severity. For example, if distinct from mood disorders and vulnerability constructs such as negative affect or neuroticism, does a latent factor defined by dimensional features of GAD predict the emergence of symptoms corresponding to other *DSM–IV* disorders such as MDD and OCD?

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