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RESEARCH PAPERS

Comorbidity Among the Anxiety Disorders

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Abstract—This paper reports on the diagnoses of 120 consecutive referrals to an outpatient research program on anxiety disorders. Patients were diagnosed according to DSM-III-R criteria using a structured interview. Patterns of comorbidity among disorders were examined using two diagnostic procedures. One procedure was based on the temporal sequence of disorders, the other on the relative interference with patient functioning. The two procedures rendered different findings, with simple and social phobia more often assigned as primary diagnosis in the temporal procedure, and panic disorder with agoraphobia most often assigned as primary interference diagnosis. Comparison of comorbidity patterns for panic disorder patients with findings from an American sample revealed no significant differences. Findings from this study are discussed in terms of their implications for assessment and research. It is suggested that the diagnostic criteria for simple phobia are somewhat problematic.

The publication of DSM-III (American Psychiatric Association, 1980), with its specific, detailed, and complex diagnostic criteria, brought major changes to the classification of the anxiety disorders. While DSM-III

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contained many exclusionary rules and a hierarchy of disorders, its successor DSM-III-R (American Psychiatric Association, 1987) is relatively free of hierarchic structure. For instance, in DSM-III a diagnosis of panic disorder was not assigned if a patient also met criteria for major depression. This exclusionary rule is dropped in DSM-III-R, largely as a result of findings that showed that panic disorder and major depression may share a common vulnerability (Breier, Charney, & Heninger, 1985; Leckman, Weissman, Merikangas, Pauls & Prusoff, 1983). The use of a hierarchical diagnostic system that discourages multiple diagnoses in individual patients precludes finding such important relationships among disorders.

In case a patient meets diagnostic criteria for more than one disorder, guidelines are needed for determining which disorder is primary and which one(s) is/are secondary or additional. Traditionally the distinction primary-secondary has been made in research on the relationship between anxiety and depression (e.g., Clancy, Noyes, Hoenk, & Slymen, 1978; Dealy, Ishiki, Avery, Wilson, & Dunner, 1981). In these studies, the disorder that is considered primary, precedes the secondary disorder. On the other hand, Barlow, DiNardo, Vermilyea, Vermilyea, and Blanchard (1986) developed a set of guidelines for assigning diagnoses wherein the distinction between primary and seondary disorders is made on the basis of interference with patient functioning. The syndrome that receives primary status causes the greatest impairment in functioning. DSM-III-R has incorporated a general rule for deciding which of several diagnoses is the "principal" diagnosis (American Psychiatric Association, 1987, p. 17). "Principal" refers to the condition that is chiefly responsible for occasioning the evaluation or admission, and may be the focus of attention or treatment.

It is generally assumed that assigning diagnoses on the basis of degree of impairment is best for treatment planning. The syndrome interfering most with the patient's functioning should be targeted first for intervention (Last, Strauss, & Francis, 1987). However, it may also be valuable to assign diagnoses on the basis of the temporal relationship between the disorders since a temporal viewpoint may provide insights into the etiology of the disorders. For instance, depression following the onset of agoraphobia, may be caused by limitations the agoraphobia is imposing on the patient. In such a case it may be better to start treatment with interventions directed at relieving the agoraphobia, even though perhaps the depression is causing most of the impairment in functioning.

As yet it is unknown whether the temporal and the interference procedures for determining primary and additional status of disorders render similar or very different findings. The first aim of the present study is to compare these two procedures. In this regard, utilizing each of these two procedures, we present patterns of comorbidity among a sample of 120 consecutive patients referred to our anxiety research project. The second aim of the study is to crossvalidate Barlow and coworkers' earlier findings on comorbidity. Barlow and colleagues (1986) found that simple and so-

cial phobia were the most frequent additional diagnoses assigned as primary anxiety disorder diagnoses. A large number of anxiety disorder patients also received additional affective disorder diagnoses. The guidelines for assigning diagnoses developed by these authors are followed exactly in the interference procedure we employed, and our study thus offers a comparison of comorbidity patterns across cultures.

METHOD

Subjects

One-hundred-and-twenty patients participated in the study. Mean age of the total patient sample was 35.4 years (SD = 10.7; range = 19–74). Mean duration of disorder was 58.2 months (SD = 62.7; range = 1–251). Fifty-nine (49%) patients were female.

Procedure

Patients referred to our research project on anxiety disorders were judged by a referring professional as possibly suffering from an anxiety disorder. Most patients were referred by psychiatric residents of the outpatient clinic of the Psychiatric Department of the University Hospital of Utrecht; some were referred by other outpatient clinics in the area, and others were self-referred. Patients were provided with written information describing the purpose of the research project and the assessment procedure. On a first visit the Anxiety Disorders Interview Schedule-Revised (ADIS—R: DiNardo, O'Brien, Barlow, Waddell, & Blanchard, 1983; de Ruiter, Garssen, Rijken, & Kraaimaat, 1987) was administered. The ADIS—R is a structured interview protocol designed for differential diagnosis among the anxiety disorders (DiNardo et al., 1983). The ADIS—R also provides screening for affective disorders, somatoform disorders, substance use, and psychotic synptoms. On a second visit a battery of psychological tests, not relevant to the present study, was administered.

Diagnosis

Diagnoses were made on the basis of DSM-III-R criteria (American Psychiatric Association, 1987). Two separate procedures for diagnosing were followed: an interference procedure and a temporal procedure.

Interference procedure. The interference procedure is based on a set of guidelines for assigning diagnoses, developed by Barlow and coworkers (1986). The procedure has been outlined in detail elsewhere (Barlow et al., 1986) and will be summarized here. The clinician makes the following decisions:

1. chooses all diagnoses for which the patient meets the basic criteria;
2. decides which diagnoses can be excluded, and
3. of those diagnoses that can be assigned, chooses which can be considered primary and which are additional diagnoses.

Decision 2 includes consideration of the functional relationship between two or more syndromes. Decision 3 includes additional consideration of the interference with functioning created by each syndrome (Barlow et al., 1986).

With respect to decision 2 it should be noted that one syndrome is excluded by a second when its symptoms are subsumed under the second syndrome. Such is the case when an agoraphobic patient reports a fear of enclosed places because there is no quick escape from such places in case of a panic attack. The simple phobia of enclosed places is considered here as part of the agoraphobia and an additional diagnosis of simple phobia is not assigned. The reason for assigning only one diagnosis is based on the functional relationship between the two syndromes: both are rooted in the fear of having a panic attack, that is, they have a common antecedent. DSM-III-R provides similar guidelines for excluding diagnoses, that is, in case of multiple diagnoses for second diagnosis must be "unrelated to" the first (e.g., see criterion B, p. 243, American Psychiatric Association, 1987).

In other cases two anxiety disorders seem to exist independently. For example, one patient reported persistent fear and avoidance of a variety of situations out of fear of having a panic attack. He also suffered from a more long-standing problem of compulsive praying in order to ward off harm to other people. This patient met criteria for panic disorder with agoraphobia and for obsessive–compulsive disorder. If two or more such independent diagnoses are assigned, the syndrome responsible for greater interference with functioning is given primary status. In this particular case, the agoraphobia was assigned primary status because it interfered more with the patient's functioning, even though the obsessive–compulsive disorder was more long-standing.

Temporal procedure. The two procedures do not differ with regard to decisions 1 and 2 of the diagnostic process. Decision 3, however, is based on the temporal relationship between the disorders, that is, the disorder that occurred first is assigned primary status; the disorder that occurred subsequently is given secondary status, and so on.

The first author conducted the interviews and assigned diagnoses, according to both procedures. The second author assigned diagnoses independently on the basis of the written information in the ADIS—R interview. All final diagnoses were assigned on the basis of consensus agreement between the two clinicians.

Results of a study on the reliability of the ADIS—R interview presented by Barlow (1985) on 125 patients show excellent interrater agreement for agoraphobia, social phobia, and obsessive–compulsive disorder (kappa between .83 and .91). Good agreement was reached in the catego-

ries of panic disorder, generalized anxiety disorder, and simple phobia (kappa between .56 and .65). Preliminary data from a separate reliability study using the Dutch translation of the ADIS—R revealed somewhat lower but still acceptable kappa's (de Ruiter, Prick, Moons, Garssen, & Beerkens, 1988). Since the sample for the reliability study was a 40-patient subsample of the total sample of 120 patients, only the categories of panic disorder and agoraphobia comprised enough patients to allow calculation of separate kappa's. Diagnostic agreement was defined as an exact match of the two primary diagnoses, using the interference procedure. Kappa was .65 for agoraphobia and .60 for panic disorder.

RESULTS

Table 1 presents the primary diagnoses assigned according to the interference procedure. One-hundred-and-thirteen patients were assigned a primary anxiety or mood disorder. Seven patients received other (mainly somatoform disorders) primary diagnoses and were dropped from the study. In Table 1 the distribution of additional diagnoses among the anxiety disorders is given for the interference procedure. As can be observed, no additional diagnosis was assigned in approximately a third of the patients with generalized anxiety disorder (GAD), panic disorder (PD), and panic disorder with agoraphobia (PDA). Rated according to DSM-III-R criteria, current severity of phobic avoidance was severe for 11 patients, moderate for 24 patients, and mild for 21 patients. Patients with a primary mood disorder almost always received one or more additional diagnoses. This finding is most likely attributable to the fact that patients were referred on the basis of the presumed presence of an anxiety disorder. As a consequence the finding of secondary anxiety disorders is highly likely in the depressive patients.

Table 2 shows the frequency of specific additional diagnoses by primary diagnosis for the interference procedure. By far the most frequently occurring additional diagnosis is simple phobia. Inspection of the data reveals that the most frequently assigned simple phobias are fear of heights, fear of dogs and cats, blood phobia, and claustrophobia. Social phobia, dysthymic disorder, and major depression were also relatively frequently assigned as additional diagnoses. Of the anxiety disorders, generalized anxiety disorder (GAD), agoraphobia without a history of panic disorder (AG), and posttraumatic stress disorder (PTSD) rarely occur as additional diagnoses. Sixteen percent of PDA patients received an additional diagnosis of mood disorder (either major depression or dysthymic disorder). This occurred in 18% of panic disorder (PD) patients, in three (33%) out of nine cases of GAD, in three (100%) out of three cases of AG, and in none of 10 cases of social phobia, simple phobia, obsessive–compulsive disorder (OCD) and PTSD.

Table 3 presents the distribution of specific additional diagnoses by primary diagnosis for the temporal procedure. Simple phobia is by far the

TABLE 1

NUMBER OF ANXIETY DISORDER CASES IN WHICH ADDITIONAL DIAGNOSIS WERE ASSIGNED (INTERFERENCE PROCEDURE)

	Primary Diagnosis (*n*)										
Number of Additional Diagnoses	Panic Disorder (17)	PDA (56)	Social Phobia (3)	Simple Phobia (3)	AG (3)	GAD (9)	OCD (3)	PTSD (1)	A.Dis. NOS (2)	Dysth. Disord. (8)	Major Depr. (8)
None	6 (35%)	23 (41%)	1	3	0	3	2	0	2	1	0
One	9 (53%)	20 (36%)	1	0	2	3	0	1	0	3	3
Two	2 (12%)	11 (20%)	1	0	0	3	1	0	0	4	5
Three or more	0	2 (3%)	0	0	1	0	0	0	0	0	0

Note. PDA = Panic Disorder with Agoraphobia.
AG = Agoraphobia without a history of panic disorder.
GAD = Generalized Anxiety Disorder.
OCD = Obsessive–Compulsive Disorder.
PTSD = Post-traumatic Stress Disorder.
A.Dis.NOS = Anxiety disorder Not Otherwise Specified.
Dysth.Disord. = Dysthymic Disorder.
Major Depr. = Major Depression.

TABLE 2
ADDITIONAL DIAGNOSES AMONG ANXIETY DISORDER CASES (INTERFERENCE PROCEDURE)

	Primary Diagnosis (*n*)										
Additional Diagnoses	PD (17)	PDA (56)	AG (3)	Social Phobia (3)	Simple Phobia (3)	GAD (9)	OCD (3)	PTSD (1)	A.Dis. NOS (2)	Dysth. Dis. (8)	Major Depr. (8)
PD				1						1	2
PDA							1			2	6
Social Phobia	1	6								2	
Simple Phobia	6	28	1	2		5		1		2	5
AG	1									1	
GAD										1	
OCD		4				1				1	
PTSD	1	1									
Dysthmic Disorder		5	1			3	1				
Major Depression	3	4	2								
Alcohol Abuse	1		1								
Alcohol Dependence		1								1	

Note. PD = Panic Disorder without agoraphobia.
PDA = Panic Disorder With Agoraphobia.
AG = Agoraphobia without a history of panic disorder.
GAD = Generalized Anxiety Disorder.
OCD = Obsessive-Compulsive Disorder.
PTSD = Post-traumatic Stress Disorder.
A.Dis.NOS = Anxiety Disorder Not Otherwise Specified.
Dysth.Dis. = Dysthmic Disorder.
Major Depr. = Major Depression.

TABLE 3
ADDITIONAL DIAGNOSES AMONG ANXIETY DISORDER CASES (TEMPORAL PROCEDURE)

	Primary Diagnosis (*n*)										
Additional Diagnoses	PD (10)	PDA (27)	AG (3)	Social Phobia (5)	Simple Phobia (53)	GAD (4)	OCD (2)	PTSD (1)	A.Dis. NOS (2)	Dysth. Dis. (2)	Major Depr. (4)
PD			1		9			1			1
PDA				3	31						3
Social phobia					7						
Simple phobia	1										
AG					2					1	
GAD					5					1	
OCD		1			6						
PTSD					2						
Dysthmic disorder	1	4		1	10	1					
Major depression	1		2	1	9						
Alcohol abuse					1						
Alcohol dependence		2									

Note. PD = Panic Disorder without agoraphobia.
PDA = Panic Disorder with Agoraphobia.
AG = Agoraphobia without a history of panic disorder.
GAD = Generalized Anxiety Disorder.
OCD = Obsessive–Compulsive Disorder.
PTSD = Post-traumatic Stress Disorder.
A.Dis.NOS. = Anxiety Disorder Not Otherwise Specified.
Dysth.dis. = Dysthymic Disorder.
Major Depr. = Major Depression.

most frequently assigned primary diagnosis here. PDA and PD also relatively frequently appear as the first disorder in the patients' lives.

In comparing Tables 2 and 3 it is apparent that simple phobia is more often given as a primary temporal diagnosis than as a primary interference diagnosis. On the other hand, PD, PDA, GAD, dysthymic disorder, and major depression are more often assigned as primary interference diagnoses.

The PD and PDA groups consisted of a sufficient number of patients to allow a comparison between our sample and the American sample of Barlow and coworkers (1986). Table 4 shows the number of additional diagnoses for PD and PDA patients in the two samples. The Yates correction factor was used in the analysis since the frequency in some of the cells was less than 10. The proportion of frequencies for number of additional diagnoses in the two samples is in agreement for both PD and PDA patients (χ^2 (3, N = 34) = 1.18, NS; χ^2 (3, N = 97) = 2.43, NS, respectively).

DISCUSSION

Our study corroborates others' findings by showing that probabilities of finding one or more additional diagnoses in individuals who meet criteria for one DSM-III-R anxiety disorder are rather high (Barlow et al., 1986; Boyd et al., 1984; Last et al., 1987). This finding has important implications for assessment and treatment. It points to the relevance of systematic interviewing to cover a wide range of possibly relevant additional disorders. In the specific case of anxiety disorders, patients often present with one major problem at the clinic, most frequently panic disorder with agoraphobia. Without the use of a structured interview, the presence of additional disorders can easily be overlooked. In our experience this is especially likely when embarrassment about the disorder occurs, as might be the case with patients having obsessive–compulsive tendencies and eating disorders.

TABLE 4

NUMBER OF ADDITIONAL DIAGNOSES FOR PATIENTS WITH A PRIMARY DIAGNOSIS OF PANIC DISORDER WITHOUT AGORAPHOBIA (PD) OR PANIC DISORDER WITH AGORAPHOBIA (PDA), COMPARED WITH AN AMERICAN CLINICAL SAMPLE[a] (INTERFERENCE PROCEDURE)

	Number of Additional Diagnoses				
Sample	None	One	Two	>Two	Total
Dutch—PD	6	9	2	0	17
American—PD	2	11	3	1	17
Dutch—PDA	23	20	11	2	56
American—PDA	20	8	9	4	41

[a] Barlow, DiNardo, Vermilyea, Vermilyea, and Blanchard (1986).

A number of studies have addressed the question of the impact of additional disorders on treatment outcome of common biological and behavioral treatments for anxiety disorders. In the case of agoraphobia, several studies have found no association between additional depression and outcome of imipramine treatment (Mavissakalian & Michelson, 1986; Zitrin, Klein, Woerner, & Ross, 1983). However, two other studies found patients with high levels of accompanying depression to improve less than patients with low levels of depression (Mavissakalian, 1987; Zitrin, Klein, & Woerner, 1980). For obssessive–compulsive patients, Foa, Grayson, and Steketee (1982) found severely depressed patients to have poor outcome in behavior therapy, compared to mildly depressed individuals. In light of these findings, and considering the pattern of comorbidity among anxiety disorder patients, we recommend mentioning number and kind of additional disorders in treatment studies of anxiety patients. For clinical practice, consideration of the temporal relationship among disorders and diagnosis based on interference with functioning each provide valuable information.

The comparison of the temporal and interference procedures revealed differential patterns of comorbidity. Simple phobia was more often assigned as the primary temporal diagnosis, and PD, PDA, GAD, dysthymic disorder, and major depression were more frequently given as the primary interference diagnosis. The pattern from the temporal procedure is in line with findings of Thyer, Parrish, Curtis, Nesse, and Cameron (1985), who found median ages of onset for simple (and social) phobia to be in the early teen years. The other anxiety disorders had median ages of onset from early to late twenties.

A somewhat remarkable finding is the presence of additional simple phobias, such as fear of heights and claustrophobia, in patients diagnosed panic disorder with agoraphobia. Many agoraphobic patients fear heights and enclosed places as part of their agoraphobia. In agoraphobic patients with additional simple phobias, however, these fears were functionally unrelated to the fear of having a panic attack. Often, these patients had had severe fear of heights or fear of enclosed places long before the onset of their spontaneous panic attacks. As such, these early simple phobias perhaps reflect a certain 'phobiaproneness' in these patients.

We found that 16% of PDA and 18% of PD patients met criteria for a current secondary mood disorder (by interference criteria). This finding is somewhat in line with findings from a large panic disorder project with 481 panic patients (Lesser et al., 1988). Eleven percent of PD and PDA patients had a current major depression, and 21% had had at least one major depressive episode after the onset of panic disorder. Although diagnostic procedures across the two studies differ, the conclusion seems warranted that secondary mood disorders are likely to occur in about 20% of panic patients.

The comparison of number of additional diagnoses for PD and PDA patients between our Dutch and Barlow and coworkers' (1986) American sample showed no significant differences. However, we did note that

Barlow and coworkers' PD and PDA patients had relatively more additional mood disorders and relatively fewer additional simple phobias. The difference with regard to the simple phobias may be caused by a difference in criteria for assignment of these diagnoses, which in turn may be attributable to a certain equivocality in the DSM-III-R criteria. On the one hand, the DSM-III-R manual states that the phobia should interfere significantly with the individual's normal routine or cause the person marked distress. On the other hand, DSM-III-R provides examples of simple phobias such as insect, mice, and snake phobias, which are very unlikely to cause significant impairment of functioning. The diagnosis of simple phobia thus becomes dependent on the circumstances of the patient: does his or her life require exposure to the phobic stimulus or can the person avoid it and thus live comfortably?

In our study the three primary simple phobics who sought help for their disorder were afraid of wind, tall buildings, and vomiting. In none of the cases of secondary simple phobia had the simple phobia caused the person to seek help. However, all these patients recognized their fears as excessive and more or less interfering with their lives. We found a 50% incidence of simple phobia among agoraphobics, which may mean that we have been too lenient in diagnosing simple phobia. The high incidence of simple phobia may then be interpreted as a high incidence of specific phobic 'fears,' not necessarily meeting DSM-III-R criteria. However, it is also possible that high rates of simple phobia are indeed associated with agoraphobia.

As was mentioned above the rate of secondary mood disorders among PD and PDA patients was slightly higher in the American sample. In general, however, the pattern of comorbidity among anxiety disorders was very similar in the two samples and, as such, provides evidence for the existence of similar comorbidity patterns across cultures.

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