Comorbidity in Panic Disorder

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The DSM-III-R\(^1\) establishes operational criteria for the identification of mental disorders as distinct diagnostic categories. It states that “There is no assumption that each mental disorder is a discrete entity with sharp boundaries (discontinuity) between it and other mental disorders.” For example, major depression and dysthymia are classified as separate categories, but there is controversy over whether these disorders differ from each other qualitatively or quantitatively. In many cases, the separation of different diagnostic categories is only justified by its clinical usefulness.

The DSM-III-R recognizes that a classification of mental disorders does not classify people, but the disorders that people have. By convention, syndromes do not identify a person, but define a disorder. Disorders are pathologic processes that affect particular and limited structures or functions within the individual; they are neither synonymous nor conterminous with the individual as a whole.\(^2\) As a result of their restricted nature, several syndromes may coexist in the same person, in some cases producing a “mosaic” effect.

The presence of concomitant disorders poses nosologic, psychopathologic, and theoretical dilemmas. Most diagnostic systems make use of exclusion criteria specifying that certain diagnoses are not permitted in the presence of another disorder or class of disorders. From a nosographic point of view, any hierarchical model presupposes that a disorder located at a higher level may be responsible for a hierarchically inferior one. Hierarchies can be correctly used when one disorder...
is shown to be caused by another or when the symptoms of a disorder are entirely subsumed by those of another disorder. As a rule, when one disorder is secondary, several psychopathologic, symptomatologic, and therapeutic aspects clearly turn out to be determined by a primary condition. At present, no definitive evidence exists for a hierarchical priority for most disorders; hence, the formulation of multiple diagnoses may appear to be the best solution.

Boyd et al\(^5\) found that when DSM-III diagnoses are assigned without exclusionary restrictions, the presence of any one disorder increased the probability of the presence of another disorder that would normally be excluded. Research and clinical practice would be improved by eliminating many of the diagnostic hierarchies that have prevented the formulation of multiple diagnoses when different syndromes occur together in one lifetime or in one episode of illness. Moreover, the presence of additional syndromes could delineate homogeneous subgroups within a major diagnostic category with each subgroup displaying its own pattern of family aggregation, course, or response to treatment.\(^4\)

**PANIC DISORDER AND THE NEUROTIC SPECTRUM**

The "pharmacological dissection" operated by Klein\(^9\) enabled clinicians to separate panic attacks and agoraphobic features from a wide array of heterogeneous disorders previously classified as neurotic. Drug treatment provided the opportunity to perceive reversible core psychopathologic features that offer a key to syndromal complexities; in fact, patients often present a welter of confusing features and it is difficult to know which of these are tightly linked to fundamental disturbances and which are secondary, inconstant reverberations.\(^6\) Yet, it also could be argued that such distinctions are artificial and merely represent the creation of an apparently homogeneous group by excluding all intermediate forms of the disorder that combine various psychopathologic dimensions with these other neurotic disorders.\(^7\) Depressive, obsessive-compulsive, and generalized anxiety features as well as depersonalization and somatoform disorders have all been reported to occur in patients with panic and agoraphobic features.\(^8,9\)

G.B. Cassano, G. Perugi, and L. Musetti (unpublished data, 1989) recently evaluated 302 patients with panic disorder (PD). In selecting this group, enlarged DSM-III-R criteria were used without the restraints of any hierarchical diagnostic schema. Comorbidity with alcohol or drug abuse, other anxiety disorders, or mood disorders did not constitute exclusion criteria even when these conditions were prominent at the moment of evaluation. The Figure presents the percentage of additional diagnoses in the sample. When evaluated without the restraints of a hierarchical schema, more than 70% of patients with PD tended to have additional concomitant diagnoses, including generalized anxiety disorder, depression, hypochondria, social phobia, depersonalization-derealization, and obsessive compulsive disorder. These findings suggest that the practice of simply listing all of the diagnoses for which a patient meets diagnostic criteria may obscure true relationships between syndromes.

In their discussion of the hierarchical structure of the DSM-III, Spitzer and Williams\(^10\) proposed the concepts of "associated features" and its "coexisting complications." An "associated feature" refers to a symptom that is a typical aspect of the clinical picture given by a more pervasive disorder. The associated symptoms would not warrant a separate diagnosis. The concept of "coexisting complication" is confusing and misleading; it refers to disorders that cannot be considered as "typical features" of the more pervasive disorders and call for a separate diagnosis. These syndromal features should be labeled "concomitant disorders." In fact, the concept of complication presupposes a causal relationship that is not clearly evident in most of the concomitant disorders that may be present before the onset of what is clinically a more significant and pervasive disorder (ie, generalized anxiety in PD, PD in major depression, etc).

Perugi et al recently have observed clear-cut differences in family loading in symptoms, and in clinical course between primary and secondary social phobia.\(^11\) On the other hand, no such differences were detected when agoraphobics were compared with secondary social phobics. It follows that social phobia, like hypochondriac ideation and conversion features (hysterical displays) occurring in the context of PD, should be considered an "associated feature."

In another study, derealization-depersonalization features started dramatically during panic attacks in 34.7% of 150 patients with PD.\(^12\) Derealization-depersonalization features persisted during the postcritical phases in a considerable number of subjects, and other subjects became chronic and resistant to treatment. In some cases, it is difficult to decide whether derealization-depersonalization should be considered as simply a component of attacks (eg, tachycardia, dyspnea, or choking) as associated features or as concomitant disorders. Certainly, PD and frequently occurring derealization-depersonalization features
prompt us to speculate on their psychopathologic meaning. Derealization-depersonalization features have been reasonably interpreted as an expression of temporalismic involvement in anxious phobic patients, however, it is difficult to establish whether the involvement of such areas represents "secondary inconstant reverberation" or is "tightly linked to a fundamental disturbance." The relationships between generalized anxiety and PD have not yet been clarified. In some cases, prolonged anticipatory anxiety perpetuated by limited symptom attacks may be misinterpreted as generalized anxiety. In some patients, however, generalized anxiety may represent a preexisting or subsequent independent condition concomitant with PD.

The tendency of patients to have more than one disorder, either cross-sectionally or longitudinally, may reveal mutual pathophysiological influences. Breier et al. hypothesized that the modification of one neurotransmitter system may alter the normal functioning of others, predisposing patients to other disorders.

**PANIC AND MOOD DISORDERS**

The relationship between anxiety and depressive disorders has been widely documented through family, clinical, and pharmacotherapeutic findings. Even so, the precise nature of the relationship between panic and mood disorders remains uncertain. Many studies have shown that PD and depression can appear in the same patient either at the same time or during follow-up. The frequency of clinically significant depression during the course of PD varies between 20% and 90%; this rate is influenced by the diagnostic criteria used, the type of anxiety disorder, the type of depression, and the length of follow-up.

It should be stressed that some of the clinical and symptomatologic characteristics of PD may contribute to an excessive formulation of the diagnosis of concomitant depression when using DSM-III-R criteria. There are, in fact, aspects of PD that can simultaneously satisfy some criteria for major depression, and it is unclear to what extent they are the expression of a genuine mood disorder. The aspects that seem most problematic in this respect are those involving secondary demoralization, panic status, and a prolonged postcritical phase.

In some PD patients, attacks and avoidance precede the onset of depressive symptoms, which appear to derive from existential limitations imposed by the PD. In such cases, the depressive phenomena are characterized by anhedonia, depressed mood, and sometimes, feelings of guilt and worthlessness. Even so, these patients maintain a certain reactivity to environmental stimuli, and severe vegetative symptoms, such as sleep, appetite and sexual dysfunctions, motor retardation, and suicidal ideation, are absent.

It is unclear whether this type of secondary demoralization should be considered a genuine mood disorder or an adjustment reaction that recovers with an improvement in panic-phobic anxiety.

In the period immediately following panic attacks, particularly those characterized by depersonalization and derealization, some patients may reach a state of deep prostration and asthenia accompanied by hypersomnia or somnolence that can last for hours or days. Some of the phenomena found in these postcritical phases are similar to those observed after convulsive episodes and partial complex seizures, although most PD patients fail to display an EEG pattern characteristic of seizure disorders. The presence of these symptomatic features during prolonged postcritical phases may account for diagnostic overlap with retarded depression characterized by hypersomnia, anergia, and difficulty in concentration. These patients resemble the "atypical depressions" described in the British literature.

In some patients, panic attacks occur without periods of remission. Patients pass from one attack to another without a postcritical phase, in a way similar to that of "status epilepticus." The psychopathologic features are similar to some forms of agitated depression or to mixed states. Patients have a high level of anxiety, anorexia, marked psychomotor agitation, insomnia, and depressive mood. A favorable response of these features to alprazolam has recently been reported by Kahn et al.

In many cases, however, depressive episodes seem to follow a course that is independent of the anxiety disorder. Depression can precede panic attacks or appear during phases of the PD when panic attacks are less frequent and avoid-
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REFERENCES


