At Issue: Hierarchical Diagnosis in Chronic Schizophrenia: A Clinical Study of Co-occurring Syndromes

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Abstract

Co-occurring or associated psychiatric syndromes (APS) such as depression, obsessive-compulsive disorder (OCD), and panic disorder have largely been hidden from view by exclusion rules that prohibit their being diagnosed in the presence of schizophrenia. This article presents data from a clinical study of APS in chronic schizophrenia and reviews the relevant literature. Thirty-seven chronic schizophrenia patients consecutively admitted to a day program were administered the Structured Clinical Interview for Diagnosis for *DSM–IV* and the Yale-Brown Obsessive Compulsive Scale symptom checklist. Exclusion rules prohibiting the diagnosis of APS were bypassed. Eighteen patients (48.6%) had one or more APS. Ten patients (27%) had major depression. Eleven (29.7%) met criteria for OCD. Four patients (10.8%) met criteria for panic disorder. These findings suggest that APS may be common in chronic schizophrenia and that there is a need to study these syndromes' clinical validity, including their treatability. A research plan to study the validity of these syndromes further is discussed.

Keywords: Schizophrenia, anxiety disorders, depression, obsessive-compulsive disorder, panic disorder, associated psychiatric syndromes, comorbidity.

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Potentially treatable psychopathological syndromes, including depression (Siris 1991, 1995), OCD (Fenton and McGlashan 1986; Berman et al. 1995*a*; Meghani et al. 1998), and panic disorder (Boyd 1986; Argyle 1990; Labbate et al. 1999) co-occur with schizophrenia in notable rates. But exclusion rules in the diagnostic system, based on ideas about the hierarchical nature of psychiatric disorders, prevent people from "seeing" these syndromes, both clinically and scientifically. They may not be diagnosed in the presence of schizophrenia because they are thought to be "better accounted for" by, caused by, or part of the schizophrenia. Undiagnosed, APS generally go untreated by clinicians. Epidemiologists may also be unsure whether to count APS as independent disorders or as aspects of the schizophrenia itself. So uncertainty about the relationship of APS to schizophrenia may affect clinical practice and the estimates of prevalence (Bland et al. 1987). The meaningfulness of APS is not yet clear, however, because their clinical validity has not been adequately explored. Hence, few studies of the biological basis of schizophrenia have taken APS into account.

We have been studying the frequency of APS in a population of chronic schizophrenia patients enrolled in a large urban continuing day treatment program. We present here clinical and phenomenological data on the first 37 patients in our sample. We discuss our findings in relation to what is known about diagnostic hierarchy in schizophrenia and also assess progress in a research plan proposed more than a decade ago by Bland and colleagues (1987) to study these phenomena.

Methods

Patients who had a chart diagnosis of schizophrenia or schizoaffective disorder gave written informed consent for a Structured Clinical Interview for Diagnosis (SCID; First et al. 1994) for *DSM–IV* (American Psychiatric

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Association 1994) with a specially trained research rater (L.P.). Evaluations were conducted in the order of each patient's most recent admission to the day program. Each patient's clinical record was reviewed and clinical staff were consulted before and after each interview.

This study was carried out at the Queens Day Center (QDC), an urban community-based continuing day treatment facility located in the Jamaica section of Queens, NY (Siris et al. 1997*a*). Referrals to QDC overwhelmingly come from local psychiatric inpatient units or shorter-stay day treatment programs. Almost all of the referrals have been hospitalized multiple times, and day treatment is felt to be necessary to prevent deterioration and/or rehospitalization. QDC emphasizes psychiatric rehabilitation in an unpressured atmosphere, and the average length of stay of discharged patients is 16 months.

Lifetime diagnoses were generated for each patient. Where there were diagnostic disagreements, consensus diagnoses were made in meetings between researchers and clinicians. In addition to the SCID, each patient was given the Yale-Brown Obsessive Compulsive Scale (Goodman et al. 1989*a*, 1989*b*) Symptom Checklist as a detailed probe for OC symptoms. Only patients with unequivocal *DSM–IV* SCID diagnoses of schizophrenia were included in the sample.

The *DSM–IV* diagnostic criteria were rigorously applied, but there were several important modifications designed to highlight the role of hierarchy in diagnosis. Exclusion rules in the SCID (and *DSM–IV*) that prevent the diagnosing of APS were bypassed. If a diagnosis would have been blocked by an exclusion rule, a note was made that the diagnosis violated the usual exclusion rule.

We set an arbitrary standard for duration of coexisting mood disorders to qualify for a diagnosis of schizoaffective disorder. *DSM–IV* requires that a mood disorder be present for a "substantial portion of the duration of the (psychotic) illness" (p. 296) but does not specify what a "substantial portion" is. We required that a mood disorder be present for one-third of the duration of the psychotic illness to count as a diagnosis of schizoaffective disorder.

Results

Forty-two patients with chart diagnoses of schizophrenia or schizoaffective disorder were examined. Thirty-seven patients met the *DSM–IV* criteria for schizophrenia. The mean age of the patients was 38.7 years (standard deviation [SD] ± 9.2). Fifteen (40.5%) were African-American, 21 (56.8%) were Caucasian, and 1 (2.7%) was Hispanic. Fifteen were female (40.5%). The patients' mean duration of schizophrenic illness was 18.5 years (SD ± 9.3).

Eighteen of the patients (48.6%) had one or more APS. Thirteen (35.1%) of these had one APS, and five (13.5%) had two APS. None had all three syndromes.

Depressive Disorders. Ten patients (27.0%) met criteria for major depression. No patients met the 33 percent criterion that we set for duration of mood disorder to qualify for a diagnosis of schizoaffective disorder.

OCD. Eleven patients (29.7%) met the *DSM–IV* criteria for full OCD. Six of these patients (16.2%) exhibited an obsessive preoccupation with a delusional idea.

Panic Disorder. Four patients (10.8%) met criteria for panic disorder (two with and two without agoraphobia). It is notable that three of the four patients with panic disorder also had OC symptoms, and the fourth had major depression.

Discussion

While there is wide agreement that schizophrenia is heterogeneous in its clinical presentation, there is also a widespread tendency to treat it as a single, unitary disorder. Additional, "nonschizophrenic" psychopathology in schizophrenia patients, such as OCD, depression, and panic syndromes, the APS considered here, is often ignored. Hierarchical assumptions underlying the diagnostic system have largely kept these syndromes hidden from view and hampered the study of their clinical validity.

Substantial rates of OCD (Fenton and McGlashan 1986; Berman et al. 1995*a*; Meghani et al. 1998), panic (Boyd 1986; Argyle 1990; Labbate et al. 1999), and depression (Siris 1991, 1995) have been documented among schizophrenia patients when these syndromes were looked at individually, and also when several APS were studied all at once (Boyd et al. 1984; Bland et al. 1987; Zarate 1997; see table 1 with this article for OCD, panic, and mixed APS, and Siris 1991 and 1995 for depression as an APS). Before *DSM–III*, "anxiety and depressive disorders" (Cheadle et al. 1978) were found in schizophrenia patients living in the community, and the patients who had these disturbances were more disabled than those without them. Soni and colleagues (1992) found that anxiety and depressive disorders were more common in schizophrenia patients living in the community than among hospitalized patients and suggested this was because living in the community created more stress. Most of these studies have determined the prevalence rates either by epidemiological methods (Boyd et al. 1984; Bland et al. 1987; Soni et al.

Table 1. Prevalence of co-occurring syndromes in schizophrenia

Authors	Sample/criteria employed	Findings			
		OC	Depression	Panic	Other findings and notes
Studies of several APS all at once					
Cheadle et al. 1978	190 SZ patients living in the community; pre-*DSM–III* categories				65.3% (n = 124) had neurotic (anxiety and depressive) Sxs. The neurotic problems were (almost exclusively) associated with social handicaps (e.g., isolation, unemployment).
Boyd et al. 1984	Epidemiological study of a community sample in 5 U.S. cities; DIS/*DSM–III* criteria	OR = 12.3	OR = 28.5	OR = 37.9	
Bland et al. 1987	Random community sample in Edmonton, Alberta, Canada; DIS/*DSM–III* criteria	59.2%, $p < 0.01$	54.2%, $p < 0.001$	29.5%, $p < 0.001$	
Garvey et al. 1991	95 psychiatric inpatients studied for coexisting anxiety disorders (18 with SZ); *DSM–III* criteria			17%	"Comorbid" anxiety in 44%, generalized anxiety disorder in 22% of SZ patients. Results did not support validity of primary/secondary distinction as it pertains to anxiety disorders. "Comorbid" patients may have better prognosis.
Soni et al. 1992	Compared hospitalized chronic SZ patients (n = 201) to a matched sample living in the community (n = 142), all over age 40; RDC diagnoses				Hospitalized patients were more disorganized and had more negative symptoms of SZ. Community patients had more anxiety and depression.
Strakowski et al. 1993	102 acutely psychotic, hospitalized first-break patients (10 patients in SZ spectrum)	13.7%		6%	The researchers studied all psychotic disorders, including major depression, making the depression category redundant. "Comorbidity" in the SZ spectrum was associated with longer hospitalization.
Zarate 1997	60 randomly selected SZ or SA outpatients, "noncomorbid" (n = 32) and "comorbid" (n = 28); *DSM–IV* criteria	6.67%		19.4%	56.7% met criteria for lifetime anxiety disorders, 30% for social phobia. Work and overall function were worse in the "comorbid" group. Data on depression were not reported.
Cassano et al. 1998	96 consecutively hospitalized, currently psychotic patients, 31 with SSD, 10 with SZ	29%		19.4%	The researchers studied all psychotic disorders, including major depression, making the depression category redundant. 58.1% "comorbidity" of SZ spectrum.

Table 1. Prevalence of co-occurring syndromes in schizophrenia (Continued)

Authors	Sample/criteria employed	Findings			
		OC	Depression	Panic	Other findings and notes
Studies of the prevalence of panic only					
Boyd 1986	5 large community samples (total n = 18,572) as part of Epidemiological Catchment Area Survey; DIS/*DSM–III* criteria			28–63%	Subjects with SZ reported different rates of panic attacks, depending on the community surveyed.
Argyle 1990	20 consecutive patients attending an outpatient clinic for maintenance treatment of chronic SZ; *DSM–III–R* criteria			35/20%	7 patients (35%) had regularly occurring panic attacks; 4 of these 7 patients (20%) met full criteria for panic disorder. Agoraphobia was present in 3 of the patients with panic attacks and in 1 without panic. Among the 13 cases with significant social avoidance, 4 (20% of the total sample) had typical social phobia, with fears of appearing anxious and being humiliated.
Cutler and Siris 1991	45 patients, mostly outpatients with SZ or SA disorder who also had operationally defined postpsychotic depression; RDC diagnoses			24.4%	11 patients had panic attacks. Did not report the number of patients meeting full criteria for panic disorder.
Labbate et al. 1999	49 consecutively admitted Department of Veterans Affairs patients; *DSM–IV* criteria			43/33%	21 (43%) with panic attacks, and 16 (33%) with panic disorder. Patients with paranoid subtype of SZ were more likely than patients with SA disorder or undifferentiated subtype to have had panic attacks or disorder.
Studies of prevalence rates for OCD and OC symptoms only					
Jahrreiss 1926	Chart review of 1,000 hospitalized and clinic patients; strict criteria for OCD (similar to *DSM–IV)* but not for SZ	1.1% (n = 11)			
Rosen 1957	Chart review of 848 hospitalized inpatients; criteria not specified for either OCD or SZ	3.5%			30 had OCD "at some time."
Fenton and McGlashan 1986	After chart review, followed up 163 hospitalized inpatients an average of 15 years later; *DSM–III–R* criteria for SZ and behavioral criteria for OC Sxs	12.9%			21 patients met 2 of 8 behavioral criteria for OC Sxs.
Bland et al. 1987	Random community survey; interviewed 2,144 community	59.2%			11 patients met criteria for OCD, statistically corrected.

Table 1. Prevalence of co-occurring syndromes in schizophrenia (Continued)

Authors	Sample/criteria employed	Findings			
		OC	Depression	Panic	Other findings and notes
	residents and found 20 with SZ; DIS/*DSM–III* criteria				
Berman et al. 1995*a*	Structured interviews of 108 chronic SZ patients' therapists at community mental health center; chart diagnoses for SZ and criteria of Fenton and McGlashan (1986) for OC Sxs	26.5/30.6%			6 patients were dropped from the analysis because they had OC Sxs before but not at the point of study assessment; 27 patients exhibited OC Sxs at time of study (26.5% point prevalence); 33 patients had OC Sxs at any time (30.6% lifetime prevalence).
Eisen et al. 1997	Interviewed 77 SZ and SA disorder clinic outpatients using SCID; *DSM–III–R* criteria	7.8% OCD (n = 6)			
Porto et al. 1997	Interviewed 50 chronic SZ patients in continuing day program for lifetime prevalences; *DSM–IV* SCID of SZ and SA disorder patients with OC Sxs and OCD	60% OC Sxs 26% OCD			Lifetime prevalences.
Meghani et al. 1998	All new admissions to an outpatient psychiatry service in a large Midwestern teaching hospital over 5 years (n = 1,458) were given structured diagnostic instrument and self-report measures. Criteria unspecified.	31.7%			61 of all SZ patients (n = 192) met criteria for OCD. OCD-SZ patients had less efficient psychosocial functioning and lower self-satisfaction. No treatment differences between the two groups noted except that OCD-SZ patients were more likely tosay that the medications they received made no difference.
Rae, unpublished[1]	Reanalysis of Epidemiological Catchment Area survey, random community survey of 5 U.S. communities; DIS/*DSM–III* criteria	23.7% OCD			
Tibbo et al. 1999	52 patients from outpatient clinics at Univ. of Alberta Medical School; SCID for *DSM–IV*	25% OCD			OC-SZ group had less negative Sxs on PANSS, shorter duration of SZ and higher level of functioning of GAF. This group also had more parkinsonism.
Studies of prevalence rates of depression in schizophrenia					
See Siris, in press					

Note.—APS = associated psychiatric syndromes; DIS = Diagnostic Interview Schedule (Robins et al. 1981); GAF = Global Assessment of Functioning; OCD = obsessive-compulsive disorder; PANSS = Positive and Negative Syndrome Scale; OR = odds ratio; RDC = Research Diagnostic Criteria (Spitzer et al. 1975); SA = schizoaffective; SCID = Structured Clinical Interview for Diagnosis; SSD = schizophrenia spectrum disorders; Sxs = symptoms; SZ = schizophrenia.

[1]Personal communication by D. Rae, August 8, 1997.

1992), through chart reviews (Fenton and McGlashan 1986), or by interviewing the patients' therapists (Berman et al. 1995*a*). This is the first wholly clinical study of these phenomena that we are aware of. Several studies of psychosis with comorbid anxiety disorders included schizophrenia spectrum patients in their samples and so are included in table 1 (Garvey et al. 1991; Strakowski et al. 1993; Cassano et al. 1998). However, these studies defined the schizophrenia spectrum differently or had small numbers diagnosed with schizophrenia, making inferences about schizophrenia difficult.

There are several important methodological weaknesses of this study. Because it is based on a clinical sample at a single treatment facility, it may be of limited generalizability. The patients who come to a day center like this one tend to be sicker and more chronically ill than other outpatient samples of schizophrenia patients. The patients in this sample had a mean duration of illness of 18.5 years (SD ± 9.3 years). Hence, because of sample bias, our findings may not represent the broad population of those with schizophrenia. Second, this study did not incorporate a control group. Many studies of APS have been done on chronic patients. High rates reported for APS in chronic schizophrenia have led to speculation that APS might play some role in the development of chronicity in schizophrenia (Bermanzohn et al. 1995).

Relationship Between APS and Schizophrenia. It is unclear whether APS are separate and distinct co-occurring, or "comorbid," syndromes or whether they are a part of the patients' schizophrenic disorders—that is, "dimensions of schizophrenia," as proposed by Opler and Hwang (1994). Bland and associates (1987) suggest that this confusion may be resolved in part by studying the clinical validity of these syndromes with a three-part research strategy to determine: (1) whether the presence of APS is associated with a difference in the clinical course of the patients when compared with the course of patients without these syndromes; (2) whether corresponding syndromes occur in higher than expected rates among the family members of patients with APS compared with the family members of schizophrenia patients without them; and (3) whether these syndromes are treatable.

Comparing the rates of APS in schizophrenia to the rates of the corresponding syndromes in the general population may also shed light on this problem. If an "associated" psychiatric syndrome occurs in schizophrenia at a rate much higher than in the general population, this would not support the idea that it is a comorbidity, or a randomly occurring convergence of two independent disorders. If a separate disorder co-occurs randomly with schizophrenia, its rate in people with schizophrenia should not exceed its rate in the general population (McGlashan 1997).

The three APS described here appear to be more common in people with schizophrenia than in the general population (Bland et al. 1987). Studies since then have supported this view (table 1). For example, two studies besides this one have reported lifetime diagnoses of OCD among schizophrenia patients of about 30 percent. Berman and colleagues (1995*a*) found a lifetime rate of OC symptoms of 30.6 percent. Meghani et al. (1998) reported a rate of 31.7 percent, making 30 percent the modal rate reported in the literature for OCD in schizophrenia. No recent study of the rate of OCD in schizophrenia has found less than 7.7 percent (Eisen et al. 1997). OCD occurs in about 2.5 percent of the general population (Karno et al. 1988).

In the decade since their paper was published, Bland and colleagues' (1987) agenda has begun to be addressed:

1. *Clinical course.* Depression (Sands and Harrow 1999; Harrow et al. 1998); OC symptoms (Fenton and McGlashan 1986; Berman et al. 1995*a*; Meghani et al. 1998); and, more generally, anxiety disorders (Zarate 1997) have been found to be associated with a worse clinical course and poorer outcomes in schizophrenia patients. To our knowledge, the effect of panic on the clinical course of schizophrenia has not been examined.
2. *Heritability.* We know of no family studies of depression in schizophrenia. There has been one family study of panic in schizophrenia (Heun and Maier 1995) and a preliminary report of data regarding the families of patients with OC-like symptoms in schizophrenia (Green et al. 1998). Both studies failed to support the hypothesis that panic and OCD were independent disorders comorbid with the schizophrenia.
3. *Treatment.* While depression in schizophrenia has been found, generally, to be responsive to pharmacological treatment (Siris et al. 1987, 1997*c*; Siris 1991), little systematic attention has been given to the treatment of OC symptoms (Sasson et al. 1997; Siris et al. 1997*b*; Bermanzohn 1999) or of panic in schizophrenia (Arlow et al. 1997; Siris et al. 1997*b*).

If APS are as common as this brief review suggests, why have they received so little systematic attention?

Hierarchical Assumptions in the Diagnosis of Schizophrenia. Hierarchical assumptions at the foundation of the diagnostic system may have stood in the way

of recognition and study of these syndromes. Surtees and Kendell (1979) defined these assumptions by saying, "Psychiatric diagnoses are arranged in a hierarchy in which any given diagnosis *excludes* the symptoms of all higher members of the hierarchy and *embraces* the symptoms of the lower members" (p. 438, emphasis in original). Hierarchical thinking has been present in virtually all systems of psychiatric nosology and has been traced back to the tendency in medicine to give each patient only one diagnosis, an approach found in 17th century medicine (Foucault 1975; Boyd et al. 1984). Jaspers (1972), who first pointed out the presence of hierarchical assumptions in psychiatry, considered it a useful convention to achieve parsimony of diagnosis among psychiatric patients, even when they had symptoms of a variety of disorders.

Hierarchical concepts were formalized in psychiatric nosology in *DSM–III* (APA 1980), where many disorders could not be diagnosed if they were "due to" a disorder higher on the hierarchy. Some anxiety disorders were excluded in this way in the presence of schizophrenia. How to determine that one disorder was "due to" another one was not specified. To capture the clinical diversity of schizophrenia patients, the framers of *DSM–IV* (APA 1994) tried to increase its flexibility by changing two conventions: (1) permitting more than one diagnosis on Axis I, and (2) changing the formulation of the exclusion rules. *DSM–IV* excludes lower diagnoses if they are "better accounted for" by a higher diagnosis. Overall, these changes appear to be a qualified success. Allowing more than one diagnosis on Axis I has been accompanied by a large number of studies of "comorbidity," evidence of a broadened awareness of the co-occurrence of many syndromes with schizophrenia. On the other hand, the change in the wording of the exclusion rules from *DSM–III* to *DSM–IV* has not been much of a change. It remains up to the clinician to explain the relationship between the schizophrenia and the excluded disorder.

If further studies support the validity of APS, additional modification may be considered in the hierarchical system of diagnosis. This might permit greater recognition of potentially treatable syndromes that appear commonly in schizophrenia.

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